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PEMPHIGUS

A SURVEY OF ONE HUNDRED AND SEVENTY PATIENTS ADMITTED TO BELLEVUE HOSPITAL FROM 1911 TO 1941

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Pusey [1] credited Hebra with the earliest clarification of the clinical picture of pemphigus as it is known today. Yet few substantial advances in the knowledge of this disease have occurred in the six decades following the death of that master of clinical dermatology. A lack of knowledge of the cause of pemphigus is undoubtedly the real stumbling block in the approach toward a rational plan of therapy.

As the severity of this disease warrants hospitalization in most cases, it affords an opportunity for careful clinical observation. It was our privilege to conduct a survey of a large series of cases in the hope that the more pressing clinical problems might be better appreciated. Perhaps some service has been done in clarifying conflicting views regarding incidence, age, sex and racial frequency, mortality rates and life expectancy. We were fortunate in accumulating a series of 170 cases, dating from 1911 to 1940 inclusive, comprising those of 72 men and 98 women. Our survey was based on information contained in the patients' charts. Cases in which the diagnosis appeared to be uncertain were evaluated on the basis of such features as rapid spread of lesions, associated loss of weight, appearance of lesions on normal skin, oral lesions and the absence of a history of drug ingestion, as well as sedimentation rates and the results of Pels-Macht tests.

After a preliminary computation the patients fell into two general groups: those who died while in the hospital and those who were dis-

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1. Pusey, W. A.: The History of Dermatology, Springfield, Ill., Charles C. Thomas, Publisher, 1933, p. 104.

charged, improved or unimproved, in the latter instance leaving the hospital through the formality of a release signature. The task of making follow-up studies of all patients discharged was by no means an easy one. Employing the home addresses appearing on hospital charts, we addressed personal letters to 74 of the patients requesting full information of their present state of health. In the event that death had already occurred a suitable postscript was added requesting the surviving relative to furnish the date and cause of death. Only one answer was obtained, and that was from a relative of a patient. The remaining letters were returned, after the usual interval, marked "addressee unknown." It was apparent that the fate of our patients could be learned only through a tedious search of death certificates filed with the registrars of records of the five boroughs of greater New York. Through the generous cooperation of Mr. Thomas J. Duffield, registrar of records, department of health of the city of New York, a report was obtained accounting for 37 patients (50 per cent of those discharged), most of whom had died within three years after leaving the hospital. Of the remaining 37 persons unaccounted for, Mr. Duffield wrote: "The fact that a death certificate is not found does not at all indicate that the person is not dead. Death may have occurred elsewhere than in the city of New York."

INCIDENCE

The year 1911 marked the institution of modern hospital records, which accounts for this limitation in our series. Pollitzer [2] offered statistics from 1898 to 1911 showing an incidence of 1 case of pemphigus vulgaris per 1,500 cases of all cutaneous diseases, a percentage of 0.066. Grace [3] reported that the disease was more common in age groups over 40, occurring equally in both sexes, and that so far as New York was concerned, 60 per cent of the cases occurred in Jews, especially those born in central and southern Europe.

The total of all patients with cutaneous diseases admitted to Bellevue Hospital during the entire period covered by the survey was not available, because until a separate dermatologic service was created in 1929, such patients were distributed among the four divisions of the hospital's medical and surgical services. From 1929 to 1940 inclusive 10,862 patients with cutaneous disease were admitted, of whom 88 had a diagnosis of pemphigus. No acute septic pemphigus was encountered. In 3 cases the condition was diagnosed as pemphigus vegetans, in 4 as pemphigus foliaceus and in 4 as pemphigus erythematodes (Senear-Usher syndrome). Table 1 presents the numbers and percentages of patients with pemphigus admitted in relation to all dermatologic admis-

2. Pollitzer, S.: Report of the Committee on Statistics of the American Dermatological Association, J. Cutan. Dis. **32**:312 (April) 1914.

3. Grace, A. W.: Pemphigus, M. Clin. North America **22**:1345-1353 (Sept.) 1938.

sions for the years indicated. These figures yield an incidence of 0.8 per cent, a value higher than that given by Pollitzer.[2]

Table 2 reveals several important facts: There were 35 Jewish men and 49 Jewish women in the entire series; the total of both sexes in this racial stock constituted 49.4 per cent of all patients admitted with pemphigus (in contrast with 60 per cent cited by Grace [3]). The Italians, 13 men and 7 women, constituted 11.7 per cent; the Negroes, 2 men and 11 women, 7.6 per cent; the Irish, 5 men and 6 women, 6.4 per cent; the Americans, 5 men and 6 women, 6.4 per cent; the Germans, 7 women, 4.1 per cent; the Poles, 3 men and 1 woman, 2.3 per cent; the Greeks, 1 man and 2 women, 1.7 per cent; the Turks, 1 man, 0.6 per cent; the Armenians, 1 man, 0.6 per cent; the Chinese, 1 man, 0.6 per cent, and unknown races, 5 men and 9 women, 8.2 per cent of all the

TABLE 1.—*Relation of Patients with Pemphigus to Patients with All Dermatologic Conditions*

Year	Patients with Pemphigus	Patients with Dermatologic Conditions	Percentage
1929	8	852	0.9
1930	12	640	1.9
1931	3	837	0.4
1932	3	955	0.3
1933	15	1,098	1.4
1934	4	1,064	0.4
1935	6	948	0.6
1936	10	1,054	0.9
1937	7	977	0.7
1938	5	998	0.5
1939	6	721	0.8
1940	9	718	1.3
Total	88	10,862	0.8

patients admitted with pemphigus. In this connection it should be stated that the patients admitted to Bellevue Hospital consist largely of Jews, Italians and Negroes. It is not unreasonable to assume that a hospital of similar capacity located in an area inhabited by a more universal group of racial stocks would show an even smaller percentage of Jewish admissions. The 35 Jewish males represented 48.6 per cent of all males admitted with pemphigus; the 49 Jewish females represented 50 per cent of all females.

The relative mortality for age groups is self evident on examinations of the columns marked totals for age groups. In the males the highest mortality occurred in the age groups 40 to 75, while in the females the highest mortality appeared in earlier age groups, 30 to 34 years, and diminished from 55 to 59 years. These values may have prognostic significance.

As regards the frequency of pemphigus, table 2 also presents the incidence based on age groups. It will be seen that the majority of the patients were in the age groups between 25 and 55 years. It is

TABLE 2.—*Mortality in Relation to Racial Stocks and Age Groups*

	Age Groups, Years	Jews		Italians		Negroes		Irish		Americans		Germans		Poles		Greeks		Turks		Armenians		Chinese		Unknown		Totals	
		L*	D*	L	D	L	D	L	D	L	D	L	D	L	D	L	D	L	D	L	D	L	D	L	D	L	D
Males																											
	10-14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
	15-19	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20-24	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1
	25-29	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
	30-34	2	1	1	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	5	2
	35-39	3	2	0	0	0	0	1	0	1	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	5	4
	40-44	1	4	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	5
	45-49	0	4	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6
	50-54	2	5	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	3	7
	55-59	0	2	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6
	60-64	0	2	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	3
	65-69	1	0	1	2	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	2	6
	70-74	0	4	1	1	0	0	0	2	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	9
	75-79	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Totals	9	26	5	8	0	2	2	3	2	3	0	0	2	1	0	1	0	1	1	0	0	1	0	5	21	51
	Percentage of patients admitted	20.5		7.6		1.1		2.9		2.9		0		1.7		0.6		0.6		0.6		0.6		2.9			
Females																											
	10-14	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	15-19	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20-24	0	1	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
	25-29	2	2	0	0	0	2	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	3	5
	30-34	0	4	1	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	8
	35-39	1	5	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	2	7
	40-44	0	3	0	0	0	0	0	2	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	6
	45-49	0	6	1	0	2	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	2	4	10
	50-54	2	11	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	3	14
	55-59	1	2	0	0	0	0	0	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1	0	4	3
	60-64	1	3	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	5
	65-69	0	1	2	0	0	1	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	3	3
	70-74	1	2	0	0	0	0	0	0	0	2	0	2	0	0	0	0	0	0	0	0	0	0	0	0	1	6
	75-79	0	1	0	0	0	0	0	1	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	4
	Totals	8	41	4	3	3	8	1	5	0	6	2	5	1	0	1	1	0	0	0	0	0	0	3	6	23	75
	Percentage of patients admitted	28.9		4.1		6.5		3.5		3.5		4.1		0.6		1.1		0		0		0		5.3			

* L = living; D = dead.

notable from these figures that pemphigus is not as infrequent in young adults as is commonly supposed.

Chart 1 is self evident and represents graphically all the patients with pemphigus according to sex and racial stock.

Chart 1.—Racial stock and sex of patients with pemphigus.

Chart 2 presents the geographic source or nativity for each patient. Particular attention is directed to the preponderance of Russian-born and American-born patients, constituting together 53 per cent of all patients admitted with pemphigus. Among the minority groups, patients born in Italy and Austria constituted equally 8.2 per cent of the admissions. The mortality for the Russian-born patients, both sexes, was 72.9

per cent, and that for the American-born patients, 80.9 per cent. While these figures are high, they are not as excessive as Schamberg [4] stated: "I have seen scores of cases in Russian, Galician or Polish Jews. What is more significant is that it is almost always fatal in such persons."

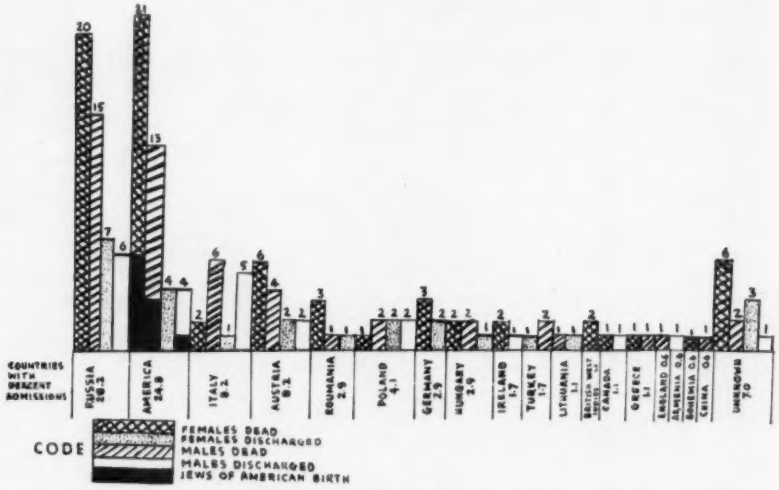

Chart 2.—Geographic source of patients with pemphigus.

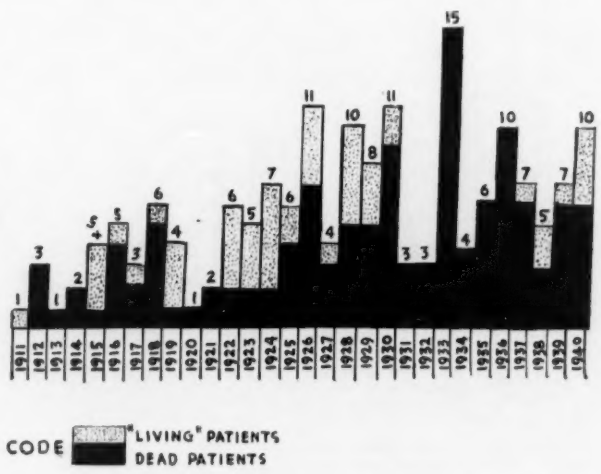

Chart 3.—The fate of all patients with pemphigus according to year of admission to hospital.

Particular attention is directed to the 10 American-born Jewish patients because they refute the experience of Schamberg, who reported seeing pemphigus but once in a Jew of American birth.

4. Schamberg, J. F.: Pemphigus: Recovery Following Long Continued Colonic Irrigations and Arsenic by Mouth, Arch. Dermat. & Syph. **25**:134-138 (Jan.) 1932.

Chart 3 shows chronologically the fate of all the patients in our series. Those indicated as "living" actually represent in most instances patients follow-up study of whom was unsuccessful. It will be noted that all patients (41) admitted from 1931 to 1936 inclusive are known to have died. Of 29 patients admitted from 1937 to 1940 inclusive, 8 are known to be alive at the time of writing. It is worthy of note that in the decade from 1911 to 1920 the lowest number of patients with pemphigus (30) were admitted, in contrast to the 70 patients admitted in the decade from 1921 to 1930 and the 70 admitted during the decade from 1931 to 1940.

SITES OF EARLIEST LESIONS

Sites of earliest lesions were considered. The most frequent early lesions were those appearing on the trunk (37.8 per cent). In several women the earliest lesions appeared on the breasts or in the mammary folds. The onset with early lesions in the mouth was next most frequent (31.9 per cent). These sites together, trunk and mouth, accounted for the earliest lesions in 69.7 per cent of the histories read. Earliest lesions appeared on the face in 9.3 per cent of the patients; on the extremities in 10.2 per cent; on the scalp in 5.9 per cent; on the neck in 1.8 per cent; in the eyes, 2.1 per cent, and, least frequently, in the groins in 1.2 per cent. In addition to the consideration of sites of earliest lesions on an anatomic basis, we noted several features in the histories which are deemed worthy of mention. The disease appeared after the following occurrences: (*a*) tonsillectomy in a 37 year old white woman, (*b*) the birth of a baby in a 32 year old white woman, (*c*) baby's bite of the nipple in a 29 year old Negress, (*d*) influenza in a 26 year old white woman, (*e*) a drinking bout in a 32 year old white man, (*f*) an attempt to extract a tooth with a nail in a 32 year old man, (*g*) swallowing of a fishbone in a 46 year old white woman, (*h*) vaccination in a 27 year old white man and (*i*) a suppurative periodontoclasia in a 37 year old white woman. In another case pemphigus was complicated by a left parasagittal spongioblastoma multiforme in a 50 year old white man.

FAMILIAL ELEMENT

Few familial cases of pemphigus have been recorded. In our series no clearcut evidence of familial involvement was found. However, a 36 year old white woman, who died later, stated that a brother-in-law had had pemphigus six months prior to the onset of her illness. Another patient, a 61 year old white woman, stated that a cousin had had the disease eighteen years before the onset of her illness and had been cured.

SYMPTOMATOLOGY AND DIAGNOSIS

During our study of the patients' charts we found signed observations and opinions of many consultants which were in conflict with our own observations. The following convictions as diagnostic criteria appeared most frequently: 1. The diagnosis of pemphigus was predicated on the patient's being a Jew. 2. The diagnosis presupposed the absence of itching. 3. The diagnosis presupposed the absence of inflammatory changes (erythematous halo) around the bullae.

The symptoms and signs most frequently noted were analyzed. Itching, while noted most frequently (59.3 per cent) in the charts of patients, is not accepted as a symptom by many dermatologists with extensive clinical experience, who call attention to the fact that objective evidence of scratching is rarely observed. Loss of weight was the most frequently recorded sign, appearing in 28.7 per cent of the patients. This value appears to be low and may be accounted for by the fact that a large proportion of charts failed to record weights on admission and during hospitalization. Burning of the skin was recorded in 20.7 per cent of the patients. Bleeding from the mouth and soreness in the mouth were recorded in 17.1 per cent. Weakness was noted in but 10 per cent; here, too, it may be stated that this figure seems to be low because it is well known that most patients with this disease soon become debilitated. Obesity to a decided extent was recorded in 10.4 per cent of the patients. Erythema around the bullae was noted in 4.7 per cent. It was further noted that loss of weight, bleeding from the mouth and soreness in the mouth appeared more frequently on the charts of patients who later died.

ASSOCIATED ILLNESSES

Fifteen charts indicated that the patients suffered associated illnesses or complications. Three patients had auricular fibrillation; 2 were pregnant, and 1 each had the following conditions: parotitis, diabetes, diarrhea, multiple sclerosis, hemiplegia, essential hypertension, left parasagittal spongioblastoma multiforme, lymphosarcoma, paralysis agitans and chronic pulmonary tuberculosis.

LABORATORY TESTS AS DIAGNOSTIC AIDS

The blood picture in pemphigus is well known. Grace [3] called attention to certain striking and consistent features: the secondary anemia and the progressive elevation of the total white cell count with the patient's deterioration and its rapid fall within the forty-eight hours immediately preceding death. In regard to the differential ratio, the shift to the left corresponding with progressive deterioration and the moderate eosinophilia occurring in the early stages and its reduction in the late stages are also recognized. In our series, blood counts and differential studies confirmed these values.

Tulipan and Director [5] studied the sedimentation rates in 13 cases of pemphigus and found increased (pathologic) values in 11 cases, a borderline value in 1 case and a normal value in 1 case. The pathologic increases in the sedimentation rates paralleled the relative toxicity expressed by the Pels-Macht index in 85 per cent of the cases.

The results of chemical examination of the blood in 20 cases were consistently normal. This observation is not offered in refutation to that of Talbott and Coombs,[6] whose studies were obviously better con-

TABLE 3.—*Pels-Macht Phytopharmacologic Indexes in Relation to Age, Sex, Extent of Lesions and Duration of Life*

Case No.	Age	Sex	Extent of Lesions	Length of Life in Days Since Onset	Pels-Macht Index, per Cent	Outcome
1	73	M	Extremities, trunk, mouth and eyes	308	58	Died
2	58	F	Breasts, mouth and groins	1,612	64	Died
3	47	F	Scalp, extremities, trunk and mouth	448	76	Died
4	43	F	Mouth, trunk and extremities	364	67	Died
5	77	F	Trunk and nose	196	47	Died
6	52	F	Mouth, trunk and vagina	378	59	Died
7	58	M	Face, trunk and mouth	322	64	Died
8	32	F	Trunk and extremities	190	65	Died
9	62	F	Eyes, face, mouth and trunk	273	53	Died
10	52	M	Face and trunk	840	45	Died
11	62	M	Mouth, trunk and groins	49	51	Died
12	34	F	Mouth, nose and extremities	98	55	Died
13	38	M	Trunk, face and mouth	50	58	Died
14	55	M	Trunk and mouth	90	66	Died
15	70	M	Trunk, extremities and mouth	50	62	Died
16	32	M	Mouth, trunk and penis	98	79	Died
17	45	F	Mouth and face	98	79	Died
18	75	F	Trunk, eyes and mouth	147	61	Died
19	67	F	Face	120	65	Died
20	43	M	Extremities	Unknown	65	Living
21	62	F	Mouth and trunk	Unknown	44	Living
22	67	M	Face and trunk	Unknown	65	Living
23	42	F	Trunk and face	1,148	59	Living
24	58	F	Trunk, extremities and mouth	224	58	Living
25	38	M	Mouth, trunk and groins	213	72	Living
26	36	M	Mouth and face	Unknown	48	Living
27	72	M	Extremities and trunk	Unknown	70	Living

trolled. In no instances in our series were blood and plasma volumes determined, nor were the serum concentrations for sodium, potassium and calcium studied in terms of milliequivalents per liter or at specified stages of the disease.

Contents of bullae of 10 patients were studied and cultured. Four cultures were sterile. Five showed Staphylococcus aureus. Fluid from bullae of 1 patient revealed streptococci and diphtheroids. Eosinophils were observed in fluid from bullae of 3 patients.

5. Tulipan, L., and Director, W.: Red Cell Sedimentation Tests in Dermatology, Arch. Dermat. & Syph. **27**:759-765 (May) 1933; personal communication to the authors.

6. Talbott, J. H., and Coombs, F. S.: Pemphigus: Experimental Studies on Thirty-Four Patients, Arch. Dermat. & Syph. **41**:359-369 (Feb.) 1940.

Perhaps more significant than other diagnostic determinations were the Pels-Macht phytopharmacologic indexes. These were obtained by mailing the blood serum of patients to Drs. Pels and Macht, who submitted the values for our information. Twenty-seven determinations were made in 27 cases of pemphigus (table 3). Values ranged from 44 per cent to 79 per cent, the average for all being 61 per cent. Pels and Macht [7] reported their observations in 233 cases, which gave an average of 58.8 per cent. In our series only 4 serums gave normal readings, the remainder being toxic. The average in the cases in which the readings were high (normal) was 74 per cent. There appears to be no specific relation between the length of life, the extent of involvement, the sex or age and the Pels-Macht index.

TREATMENT

A survey of the treatment employed for a large series of patients with any disease for a thirty year period is in itself a veritable history of therapeutics. The metamorphosis, as we found it, in the treatment of pemphigus runs parallel with the progress which the medical profession has made in general. As each new drug was discovered and introduced to medicine the hopes for cure found new enthusiasm; so it has been with the drugs proposed for the treatment of pemphigus.

In general, the treatment administered can be divided into five groups: (1) stimulants, (2) specific remedies, (3) drugs for local application, (4) vitamins and (5) miscellaneous drugs (table 4). In the evaluation of these methods of treatment it is apparent that in view of their great variety a single criterion is necessary. The fact that a patient is recorded as living by no means indicates that the treatment was curative or even life-prolonging, because many patients recorded as living (in cases in which follow-up studies were unsuccessful) might, in reality, have died. The remaining factor, the average length of life of patients who died, offers the best measuring stick for gaging the value of any stated treatment.

Calculations of the average length of life did not take into account the period before hospitalization for several reasons: 1. The patient's memory of the time of onset was often unreliable. 2. The patient might have been unaware of the earliest lesions, especially when they appeared in the mouth. 3. Some patients were not hospitalized until the disease was in the terminal stage, having lived at home for practically the entire duration of their illness. Obviously the treatment given to patients who lived for a short time in the hospital can hardly be evaluated on the basis of the period of illness before hospitalization.

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7. Pels, I. R., and Macht, D. I.: Phytopharmacologic Test in Pemphigus: Further Studies, Arch. Dermat. & Syph. **29**:206-218 (Feb.) 1934.

The average length of life after hospitalization for all patients who received stimulant treatment was ninety-four and nine-tenths days; specific treatment, one hundred and six and six-tenths days; miscellaneous treatment, one hundred and thirty-seven and one-tenth days; vitamins, thirty and six-tenths days, and local treatment, only thirty-six and two-tenths days. The average length of life of patients receiving no treatment was sixteen days. Obviously these gross averages offer only approximate and comparative information. The highest average, one hundred and thirty-seven and one-tenth days—that for the miscellaneous group of treatments—was influenced by a single patient who received a high caloric diet and calcium gluconate and lived seven hundred and ninety-one days. Elimination of this patient's data and recalculation would yield an average length of life of eighty-two and seven-tenths days. More significant than these group averages are the average figures for each specific treatment.

Seven patients who died received various types of stimulant treatment during the period 1911 to 1928 inclusive. Of this group 2 patients were treated with caffeine with sodium benzoate and lived an average of ninety-two days. One patient received the combination of caffeine with sodium benzoate and strychnine sulfate and lived for three hundred and ninety-two days. Three patients were treated with digitalis (digitalis and strychnine in 1 case) and lived an average of thirteen days. One patient received epinephrine hydrochloride and lived forty-nine days.

Fifty-six patients who later died received various drugs classed as specific during the period 1914 to 1940 inclusive. Sixteen patients of this group received solution of potassium arsenite U. S. P. and lived an average of ninety-four days. Two patients treated with this solution and cod liver oil lived an average of sixteen days. Two patients given solution of potassium arsenite U. S. P. and strychnine lived an average of four days. One patient treated given solution of potassium arsenite U. S. P. and quinine lived for eighty-four days, while another who received solution of potassium arsenite U. S. P., autohemotherapy, blood transfusions and a salt-poor diet lived one hundred and forty days. Three patients treated with sodium arsenate and autohemotherapy lived an average of one hundred and forty-six days. Two patients who received iron cacodylate and coagulin (a blood coagulant), as suggested by Davis and Davis,[8] lived an average of twenty-one days. Four patients received neoarsphenamine and lived an average of fourteen days. Three patients were treated with acetarsone and supplementary treatment; 1 lived three hundred and sixty-five days and 2 an average of seventy-four days. Two patients received tryparsamide (with other treatment) and

8. Davis, R. H., and Davis, W. D.: A Contribution to the Treatment of Pemphigus, Arch. Dermat. & Syph. **8**:617-633 (Nov.) 1923.

lived an average of twenty-four days. One patient was treated with aldarsone (a pentavalent arsenical, sodium methylenesulfonamino-hydroxyphenylarsenate) and lived an average of three days. Another was given aldarsone and supplementary treatment and lived eighty-four days. Two patients treated with methylthionine chloride lived an average of two hundred and three days, and 1 patient who received this drug and sodium cacodylate lived three hundred and seventy-one days. Two patients who received moccasin snake venom and supplementary treatment lived an average of four hundred and forty-nine days. Five patients who were treated with germanin and supplementary treatment lived an average of one hundred and twenty-eight days. Six patients received sulfanilamide (1 also received acetarsone) and lived an average of eighty-nine days. Two patients treated with adrenal cortex extract lived an average of eighty days. Three additional patients who received this drug remained alive and to the date of writing have lived an average of two hundred and eighty days.

Thirteen patients who died received a variety of treatments and were classified in the miscellaneous group. One patient received quinine and lived seven days. Two patients received high caloric diets and lived an average of eight days. Two patients treated with liquid spleen and solution of potassium arsenite U. S. P. lived an average of twenty-eight days. Three patients who received autogenous vaccine and solution of potassium arsenite U. S. P., digitalis and sodium cacodylate lived an average of eighty-six days. One patient was treated with spinal cord vaccine and lived for one hundred and five days. One patient who received potassium iodide lived for one hundred and sixty-eight days. Two patients were given blood transfusions and lived an average of one hundred and ninety-one days. One patient who was treated with a high caloric diet and calcium gluconate lived seven hundred and ninety-one days.

Fourteen patients who died received vitamins during the period 1933 to 1940. Of this group 4 patients were treated with viosterol in oil and solution of potassium arsenite U. S. P. and lived an average of fifty days. One received viosterol in oil alone and lived eleven days. Six patients who received a high vitamin diet (3 were also given solution of potassium arsenite U. S. P.) lived an average of twenty-nine days. One patient who was given injections of liver extract lived twenty-six days. One patient received nicotinic acid and lived six days. One patient who received cod liver oil lived eleven days.

Chart 3 represents all patients admitted by years including both "living" and dead. Many of the columns from 1911 to 1930 show patients classified as "living" simply because follow-up efforts to confirm their deaths were unsuccessful. The treatment employed during this period can hardly be interpreted as curative or successful. On the

TABLE 4.—*The Value of Various Types of Treatment of Pemphigus, According to Average Length of Life of Patients Who Died*

Year	Treatment Administered	Number of Patients	Number of Patients Who Died	Average Stay in Hospital of Discharged Patients, Days	Average Life After Hospitalization of Patients Who Died, Days
	Stimulants				
1911-1920	Caffeine with sodium benzoate	2	2	..	92
1911-1920	Caffeine with sodium benzoate and strychnine sulfate	1	1	..	392
1921	Strychnine and digitalis	1	1	..	21
1922	Iron, quinine and strychnine	1	0	7	..
1924	Digitalis	3	2	18	9
1928	Epinephrine hydrochloride	1	1	..	49
	Specific Remedies				
1914-1940	Solution of potassium arsenite U. S. P.	21	16	16	94
1915	Solution of potassium arsenite U. S. P. and potassium iodide	1	0	7	..
1916	Solution of potassium arsenite U. S. P. and strychnine	2	2	..	4
1916	Solution of potassium arsenite U. S. P. and cod liver oil	2	2	..	16
1917	Solution of potassium arsenite U. S. P. and quinine	1	1	..	84
1931	Solution of potassium arsenite U. S. P., autohemotherapy and salt-poor diet	1	1	..	140
1915	Neoarsphenamine	5	4	35	14
1919	Sodium cacodylate and solution of potassium arsenite U. S. P.	1	0	14	..
1919	Sodium cacodylate	1	0	7	..
1923	Acetarsone and stool vaccine	1	1	..	365
1924	Acetarsone and solution of potassium arsenite U. S. P.	2	2	..	74
1924	Sodium arsenate and autohemotherapy	3	3	..	146
1925	Iron cacodylate and coagulin	3	2	28	21
1929	Tryparsamide and solution of potassium arsenite U. S. P.	1	1	..	28
1930	Tryparsamide and blood transfusions	1	1	..	21
1933	Methylthionine chloride	3	2	126	203
1933	Methylthionine chloride and sodium cacodylate	1	1	..	371
1933	Moccasin snake venom, acetarsone and methylthionine chloride	2	2	..	449
1935	Germanin, methylthionine chloride and sodium arsenate	7	5	85	128
1937	Sulfanilamide	6	5	140	90
1938	Acetarsone and sulfanilamide	1	1	..	84
1938	Aldarsone	1	1	..	3
1939	Aldarsone, germanin and mapharsen	1	1	..	84
1940	Adrenal cortical extract	5	2	280	80
	Miscellaneous Drugs				
1915	Potassium iodide	1	1	..	168
1916-1923	Autogenous vaccine, solution of potassium arsenite U. S. P., digitalis and sodium cacodylate	3	3	..	86
1923	Old tuberculin	2	0	140	..
1928	Blood transfusions	4	2	10	191
1929	Autohemotherapy and blood transfusions	1	0	28	..
1930	Quinine	1	1	..	7
1930	High caloric diet	2	2	..	8
1930	Liquid extract of spleen and solution of potassium arsenite U. S. P.	3	2	14	28
1930	Amniotin	1	0	14	..
1934	High caloric diet and calcium gluconate	1	1	..	791
1936	Spinal cord vaccine	1	1	..	105
	Vitamins				
1933	Viosterol in oil and solution of potassium arsenite U. S. P.	4	4	..	50
1934	Viosterol in oil	1	1	..	11
1934	High vitamin diet and solution of potassium arsenite U. S. P.	3	3	..	30
1934	High vitamin diet	3	3	..	28
1934	Cod liver oil	1	1	..	11
1936	Liver extract	1	1	..	26
1940	Nicotinic acid	1	1	..	6
	Local				
1922-1932	Boric acid ointment and calamine lotion	33	24	8	36
	No treatment	20	15	7	16

other hand, reference to the columns for the years 1931 to 1940 yields information which is more accurate. For one thing, follow-up studies were more successful. With the exception of 3 living patients (2 discharged in 1938 and 1 in 1937) every patient is accounted for. The 1939 living patient received only local therapy. The most significant column is that for 1940. Six patients are dead and of the 4 remaining

TABLE 5.—*Follow-Up Studies of Patients Who Died*

Patient	Duration of Illness After Onset, Days	Duration of Life After Discharge, Days	Reading on Death Certificate
1	151	1	Pemphigus
2	63	14	Pemphigus; peritonitis; pneumonia
3	21	385	Pemphigus; acute nephritis
4	154	28	Pemphigus; chronic nephritis
5	42	256	Pemphigus
6	126	70	Myocarditis with decompensation
7	283	8	Pemphigus
8	44	1	Pemphigus
9	203	175	Pemphigus; bronchopneumonia
10	371	14	Pemphigus; chronic myocarditis
11	18	20	Pemphigus; cardiac dilatation
12	19	49	Pemphigus
13	147	14	Pemphigus
14	47	7	Pemphigus; chronic nephritis
15	43	2	Pemphigus; acute nephritis
16	567	28	Pemphigus; chronic myocarditis
17	175	77	Pemphigus; chronic nephritis
18	145	21	Pemphigus
19	144	30	Pemphigus
20	749	3	Pemphigus
21	42	270	Pemphigus
22	119	56	Carcinoma of the right kidney
23	196	112	Pemphigus; chronic myocarditis
24	255	44	Pemphigus; pneumonia
25	158	539	Pemphigus
26	533	4	Pemphigus
27	1,584	126	Pemphigus; left parasagittal spongioblastoma multiforme
28	300	84	Pemphigus; pneumonia
29	112	728	Mediastinal tumor
30	189	56	Pemphigus; nephritis complicating pregnancy
31	1,232	171	Pemphigus; bronchopneumonia
32	91	1,008	Ruptured esophageal varices; hematemesis
33	119	70	Pemphigus; paralysis agitans
34	84	42	Pemphigus
35	96	16	Pemphigus
36	120	21	Pemphigus
37	156	14	Pemphigus

alive, 3 were treated with desoxycorticosterone acetate and to the time of writing have lived an aggregate of eight hundred and forty days, an average of two hundred and eighty days per patient.

The following figures represent the average duration of life in days since the appearance of the earliest lesions, based on the patients' histories: the lowest figure was twenty-eight days for the years 1912 and 1913, an average of 4 patients; the highest average, obtained from 3 patients, was five hundred and fifty-eight days in 1932. For the thirty year period the average duration of life for all patients who died was two hundred and nineteen days.

FOLLOW-UP STUDIES OF PATIENTS DISCHARGED

Table 5 summarizes the data for the 37 patients follow-up studies of whom were successful. All of these patients had died. The duration of illness after onset for each patient varied from eighteen to one thousand, five hundred and eighty-four days. The average duration of illness after onset was two hundred and forty days. The duration of life after discharge from the hospital varied from one to one thousand and eight days. The average duration of life after discharge from the hospital was one hundred and twenty-three days.

The death certificates of 4 patients did not include the diagnosis of pemphigus; these deaths were attributed to the following diseases: (1) myocarditis with decompensation, (2) carcinoma of the right kidney, (3) mediastinal tumor and (4) ruptured esophageal varices and hematemesis. The death certificates of 16 patients showed pemphigus as the only cause of death. The death certificates of 17 patients showed one or more associated causes of death.

NECROPSIES

Necropsies were performed in 9 cases. In 6 the adrenals were recorded as normal. In 1 of these cases the kidneys were enlarged and pathologic changes were characteristic of acute glomerulonephritis (the treatment had been germanin). In 2 cases there was autolysis of the adrenals and hyperemia of the medulla. In 1 case the adrenals were enlarged and the cortex was yellowish, thickened and nodular. Chronic passive congestion and fatty infiltration of the liver were observed in 8 of the 9 cases.

SUMMARY AND CONCLUSIONS

The records of one hundred and seventy patients with pemphigus admitted to Bellevue Hospital from 1911 to 1941 were reviewed and analyzed.

The incidence of pemphigus in all patients with dermatologic conditions admitted to Bellevue Hospital over a twelve year period (1929 to 1941) was 0.8 per cent.

The frequency of pemphigus was found to be highest for males between the ages of 35 and 55 and for females between the ages of 25 and 55. The relative mortality was highest for males from 40 to 75 and for females from 30 to 55.

The percentage representation for all patients on the basis of nativity was calculated. The greatest number of patients were born in Russia (28.9 per cent) and in the United States (24.8 per cent). Contrary to general belief, 10 of the Jewish patients were American born.

The trunk was the most frequent site of onset of lesions of pemphigus; the mouth was the second most frequent site of onset.

Several cases suggested a familial or a contact factor in causation.

Contrary to accepted opinion, itching was found to be a common symptom of pemphigus, so far as chart records were concerned. This observation is not borne out in the clinical experience of most dermatologists; the uniform absence of excoriations confirms this.

Laboratory determinations are of distinct aid in the diagnosis of pemphigus. In the series reported, blood counts, sedimentation rates and Pels-Macht indexes were consistently representative of the disease.

All treatments administered over the thirty year period were analyzed.

The follow-up studies of 37 patients who died were analyzed.

Analysis of necropsies performed on 9 patients revealed pathologic involvement of the adrenals in 3. The liver in all 9 showed fatty infiltration and passive congestion.

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PEMPHIGUS

REPORT OF SEVENTY-SEVEN CASES.

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This is a report on 77 patients with pemphigus treated in the dermatologic service [1] of the New York City Hospital during the past twenty years.

The cause of pemphigus is still unproved, and practically all therapeutic measures have thus far been empiric. Opinions vary concerning the prognosis of this disease. There are many dermatologists who believe that all patients with true pemphigus die within a short period after onset of the disease (the time varying from a few months to some years), although they admit that remissions may occur during this period. They believe that so-called cured conditions or conditions of longer duration are not pemphigus but are bullous eruptions of dermatitis herpetiformis, erythema multiforme, lupus erythematosus disseminatus or drug eruptions. We therefore felt that this presentation containing data obtained from cases of pemphigus, such as race, previous history, symptoms and signs, laboratory findings, results of biopsies, duration and progress of the disease, response to various therapeutic measures and autopsy observations, would be of interest.

CLINICAL OBSERVATIONS

It is interesting to note that of a total of 77 patients, 56 (72.7 per cent) were Jews and 21 (27.3 per cent) were gentiles (of the total number of patients admitted yearly to the eleven hundred bed hospital about 8 per cent are Jews). Twenty-seven (48.2 per cent) of the Jews with pemphigus were born in Russia; 5 (8.9 per cent) were American, of whom 4 were of Russian extraction and 1 of Polish extraction; 11 (19.6 per cent) were born in Austria; 4 (7.1 per cent) were Polish; 4 (7.1 per cent) were Hungarian; 2 (3.5 per cent) were Rumanian, and 1 (1.8 per cent) was Italian, 1 English and 1 German. Of the 21 gen-

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1. Many of these patients were observed and treated by Drs. John A. Fordyce, William S. Gottheil, Jerome Kingsbury and A. Benson Cannon.

tiles, 6 (28.5 per cent) were American (2 of whom were colored), and 10 (47.6 per cent) were born in Italy, 2 (9.5 per cent) in Poland, 2 (9.5 per cent) in Germany and 1 (4.8 per cent) in Ireland. During this twenty year period 4 (5.1 per cent) white gentile Americans were admitted to the hospital with a diagnosis of pemphigus; the diagnosis was questionable in 2 of their cases.

In this series of cases there were no family histories of pemphigus.

There were 48 (62.3 per cent) females and 29 (37.6 per cent) males. The age incidence varied considerably. The youngest patient in our series was 17 years of age and the oldest 78.

The occupations were varied and apparently had no significance. Most of the patients were in good health prior to the appearance of the cutaneous lesions, but a few had concomitant diseases which were recognized on admission or found at autopsy.

There was a wide variation in the duration of the disease, but in many cases it was less than one year. Some of the patients had the eruption continuously for periods of from two to three years without remission.

The initial lesions occurred almost anywhere on the body and were most frequent in the mouth, on the face and on the upper and anterior part of the trunk. The percentage of oral lesions in this series of cases increased as the disease progressed, so that 51 patients (66.2 per cent) had oral lesions some time during the course of the disease. Of the 26 patients who did not have lesions in the mouth, 14 eventually died and 12 were discharged with the condition unimproved, improved or clinically cured. In 1 case, in addition to oral lesions, the patient had lesions scattered over the entire body and on the mucous membranes of the nose and rectum. Another patient, on the second admission, had bullae on the cornea and sclera of the left eye, in addition to lesions on the trunk.

The various conditions in this series were diagnosed on admission as acute pemphigus, pemphigus vulgaris, pemphigus foliaceus or pemphigus vegetans. It was observed that the acute type sometimes became chronic and that pemphigus vulgaris sometimes became foliaceous. In many of the cases the disease had to be differentiated from dermatitis herpetiformis, drug eruption, erythema multiforme or allergic dermatitis. In 2 cases the diagnosis on admission was pellagra; the condition did not respond to vitamin and liver therapy, and as the disease progressed a diagnosis of pemphigus was made. One case had been demonstrated eleven years previously as one of dermatitis herpetiformis. In another case the diagnosis was pemphigus of the eyelids and eyeballs; in this case there were also a few lesions on the mucous membranes of the mouth and on the trunk.

Fifteen patients in the group had remissions varying from a few weeks to many years. Four of the 15 had remissions twice. All of the patients who had remissions eventually died with a diagnosis of pemphigus. One patient stated that blisters had occurred in his mouth ten years previously and that he had been treated for pemphigus at that time. He had had no lesions for ten years, but at the end of this time he was readmitted to the hospital and subsequently died of pemphigus vulgaris.

The temperatures were fairly low varying from 99 to 101 F. When a complication occurred, such as renal infection or bronchopneumonia, the temperature was greatly increased. In 1 case the temperature was subnormal during the entire period of hospitalization.

Nikolsky's sign could be elicited most frequently in cases of pemphigus foliaceus. In 3 cases of pemphigus vulgaris and in 1 of pemphigus foliaceus, Nikolsky's sign could not be elicited.

The concomitant diseases which were present in some of the cases were arteriosclerosis, cardiac and renal diseases, diabetes mellitus and disease of the gallbladder. Dental caries, with or without pyorrhoea alveolaris, was present in every case of this series and in many instances was severe. In 3 cases active syphilis was present.

POSTMORTEM OBSERVATIONS

Eleven autopsies were performed, and the observations were essentially normal, even in cases in which there was a profound toxemia. In 1 case active pulmonary tuberculosis was found. In a second case the cystic duct showed obstruction and the presence of periduodenal adhesions. In a third case the liver, spleen and adrenal glands were enlarged. Microscopic examination of sections of these organs showed no definite pathologic changes.

LABORATORY DATA

Routine red and white blood cell counts, urinalyses and Wassermann tests were performed in the majority of cases. In most of them there was a slight anemia. In 5 cases the red blood cell count was over 5,000,000 per cubic millimeter but the hemoglobin content ranged from 45 to 75 per cent. The white blood cell count ranged from 6,000 to 18,000 per cubic millimeter, and in 1 case it was 25,000. The differential count in the majority of cases showed little deviation from the normal. The percentage of eosinophils averaged from 1 to 8, in 2 cases it was 15 and 20.

The Wassermann reaction of the blood in 3 cases was reported as 4 plus, and in 1 case that of the spinal fluid was 4 plus and the colloidal gold curve was tabetic.

In most instances the urine was normal, except when concomitant renal disease was present or when pemphigus was in the terminal stages. Examination of feces was made in 3 cases, with negative results. Chemi-

cal examination of the blood was made in 31 cases, and the results were found to be normal. Blood cultures were made in 17 cases and were negative. The icteric index in 3 cases was within normal limits.

The basal metabolic rate was determined in 2 cases; in 1 it ranged from + 20 to + 36 per cent, and in another it was + 55 per cent. Cultures of material from bullae were made in 8 cases, with a growth of staphylococci in 6 and no growth in 2.

The Pels-Macht test (phytopharmacologic index) was made in 3 cases; in 1 the index was 65 per cent, and in 2 the toxic reaction did not conform to pemphigus. All 3 patients died of pemphigus.

Roentgen ray examination of the chest and of the gastrointestinal tract was made in a few cases, and the results were reported as normal.

In 1 case the histologic examination of a lesion on the vulva showed chronic dermatitis; of a lymph node in the groin, chronic adenitis, and of a granulomatous lesion on the foot, a picture consistent with pemphigus vegetans. In another case histologic examination of the skin was reported as showing chronic dermatitis.

TREATMENT

All of the 77 patients received high carbohydrate diets. Topical medication consisted of: baths containing potassium permanganate, tannic acid or starch; antipruritic and antiseptic lotions, salves, and powders. Foci of infection, such as teeth and tonsils, were removed in many instances, and treatment was given for pyorrhea when present.

Vitamins.—In 1 case nicotinic acid was used orally in 100 mg. doses twice daily for four weeks. In the beginning there was slight improvement in the eruption and in the general health of the patient, but this was of short duration. In 2 cases vitamin B complex in fairly large doses was administered for a few weeks, without any noticeable improvement. In 4 cases 2 cc. of a solution of ascorbic acid was given intravenously twice weekly for two to six weeks, with no improvement. Vitamin D was used in 11 cases; in 9 of these the patients died. One patient received 50,000 U. S. P. units of vitamin D in the form of viosterol in oil orally daily for thirty-four days. At the same time large amounts of sulfanilamide were given. This patient received other therapy in the form of liver extract (intramuscularly), small doses of roentgen rays, autohemotherapy and estradiol benzoate. Therefore, it is difficult to evaluate the efficacy of each medication. The patient was discharged as improved, although many lesions of the skin were still present. One patient whose condition was not definitely diagnosed as pemphigus was in the hospital approximately three months and besides general systemic treatment received 2 cc. of viosterol in oil three times daily. Another patient received viosterol in oil in large doses, without improvement.

Sulfanilamide.—This drug was given orally in fairly large doses to 10 patients. Four patients were discharged as improved; 1 was discharged with the condition unchanged, and 5 died. One patient improved on two different occasions when sulfanilamide was first given; the first remission was of eight months' duration, and the second remission after sulfanilamide therapy was of short duration. As previously stated, 1 patient received large doses of viosterol in oil in addition to 40 grains (2.6 Gm.) of sulfanilamide in divided doses for fifteen days. This patient also received three courses of Dee's treatment, 80 grains (5.2 Gm.) of sulfanilamide daily in divided doses for the first two days, 60 grains (3.9 Gm.) daily for the next three days and 40 grains daily for the next five days). One patient received 20 grains (1.3 Gm.) of sulfanilamide every six hours for one day, 15 grains (1 Gm.) every six hours for three days and 10 grains (0.65 Gm.) every six hours for two days. There was no noticeable improvement with this therapy. One patient was in the hospital for eleven days and received small doses of sulfanilamide during this time, without improvement. One patient received 10 grains of sulfanilamide four times daily. After three days a sulfanilamide fever developed and the treatment was discontinued. There was no improvement during sulfanilamide therapy. One patient received sulfanilamide for ten days in small doses, without improvement. This patient had previously received the same drug at Bellevue Hospital with no improvement. One patient was given 375 grains (24.4 Gm.) of sulfanilamide in divided doses, without improvement. Its administration was discontinued, and the patient improved after the ingestion of solution of potassium arsenite U. S. P.

Arsenicals.—Old arsphenamine, neoarsphenamine or sulfarsphenamine was given in 11 cases. One patient received weekly injections of 0.3 Gm. of neoarsphenamine intravenenously during the last eight weeks of hospitalization. All of the lesions disappeared, and the patient was discharged free from clinical manifestations. Previously she had received large doses of solution of potassium arsenite U. S. P. orally and sodium thiosulfate intravenously, without improvement. Sulfarsphenamine was used in 2 cases with negative results. In 1 case acetarsone was used with no improvement. One patient had concomitant syphilis and was given therapy consisting of a bismuth compound and old arsphenamine. There was no improvement of the pemphigus. The other patients treated with arsenicals either became worse or showed no improvement.

Solution of Potassium Arsenite U. S. P.—This solution was given orally in 11 cases. One patient received fairly large doses without improvement. Seven years previously this same patient had received this therapy for an eruption which was diagnosed as pemphigus, and he stated that the cutaneous lesions had disappeared within a few weeks.

One patient received 6 drops of the solution three times daily for eighteen days and was discharged slightly improved after this therapy. Another patient responded to moderate doses of the solution and was discharged much improved. A third patient received the solution with no improvement. Subcutaneous injections of solution of sodium arsenate were then given, starting with 2 minims (0.12 cc.) daily and increasing to 19 minims (1.2 cc.) daily. After eighteen days this therapy was discontinued, as the patient showed no improvement. Two days prior to death he also received sulfanilamide orally and injections of a blood coagulant (coagulen) and boiled liver extract.

Sodium Thiosulfate.—This drug was given intravenously in 16 cases in doses of 15 grains (1 Gm.) for from ten to thirty injections. In 1 case there was improvement. This patient had a complete remission on two different occasions with this medication. Fifteen patients showed no response to this therapy.

Quinine.—Quinine was administered orally in 5 cases. One patient was discharged as cured after receiving 2 grains (0.13 Gm.) three times daily for forty-seven days. Other therapy which this patient received was a high caloric and high vitamin diet. One patient was given 10 grains (0.65 Gm.) of quinine three times daily for one month. The patient became progressively worse and died. Plasmochin, a synthetic quinine, was used in 3 cases with no improvement.

Coagulen.—Coagulen (a hemostatic preparation made from blood platelets) was given in 11 cases. One patient received 20 cc. of a 3 per cent solution intramuscularly every other day, alternating with 1 grain (0.065 Gm.) of iron cacodylate intravenously every other day (Davis and Davis treatment) for thirty injections of each medication. During this therapy he showed great improvement. On his second admission injections of coagulen were discontinued, as they made the patient uncomfortable. A second patient received 20 cc. of a 3 per cent solution of coagulen intramuscularly biweekly for fifteen injections, without improvement. A third patient received 20 cc. of a 3 per cent solution of coagulen intramuscularly, along with 1 grain of iron cacodylate intravenously, for five injections of each, with some improvement. None of the other patients receiving coagulen showed improvement.

Moccasin Snake Venom.—This drug was given in 3 cases. During the second admission 1 patient received twenty injections of moccasin venom but became progressively worse. Another patient received nine injections at five day intervals, beginning with 0.1 cc. and increasing to 1 cc. Some improvement was noted. A third patient was given two injections of moccasin venom and in addition received 40 drops of viosterol in oil three times daily, without improvement.

Germanin.—Four patients received germanin without any noticeable improvement (the average dosage is 0.5 Gm. for four to six doses). One patient became worse under this therapy. Another patient received, in addition to injections of germanin, sulfanilamide, sodium thiosulfate and liver extract during the six weeks period of hospitalization. This patient left the hospital unimproved.

Acriflavine.—One patient received nine injections of 0.3 Gm. of neutral acriflavine at five day intervals. This was dissolved in 30 cc. of physiologic solution of sodium chloride and was given intravenously. After the sixth injection the patient had severe abdominal pain, which disappeared within a short time. He received three more injections of acriflavine and was discharged from the hospital with a disappearance of his lesions.

Miscellaneous Treatments.—Other therapy used in our group of cases included autohemotherapy and the administration of a bismuth compound, calcium gluconate, potassium chloride, sodium citrate, calcium thiosulfate, colloidal manganese, atropine sulfate, iodides, insulin, foreign protein (sterile milk and typhoid vaccine), estrone (theelin), estradiol benzoate and a 1 per cent solution of mercurochrome, 15 cc. intravenously. No improvement followed the use of any of these medications.

One patient had been treated at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, where she received almost every conceivable treatment for pemphigus, including solution of potassium arsenite U. S. P., arsphenamine, ferric iodide, estrone (theelin) and various external medications, without improvement.

In 1 case serum from the blood of another patient with pemphigus was injected into the buttocks on four different occasions, without improvement. In a second case 3 cc. of whole blood from a patient with pemphigus was injected intramuscularly for three injections at weekly intervals, with no improvement. In a third case serum was taken from bullae and injected intracutaneously in one arm. In the other arm physiologic solution of sodium chloride was injected intracutaneously. Several new blebs formed on the sites of the injections of the serum. The control sites were normal. Further treatment given this patient was the withdrawal of 10 cc. of blood and the injection of the serum intracutaneously. The patient became progressively worse.

Repeated transfusions in cases in which the condition was more toxic gave some improvement, which was of short duration.

One patient was treated in the New York Hospital with a preparation of mouse brain which had been inoculated with pemphigus material. This preparation was administered intravenously without improvement.

Ultraviolet radiation was given to many of these patients, with a temporary improvement in 2. One patient received forty treatments

with ultraviolet radiation over the entire body. At the beginning of this treatment there was some improvement, which was of short duration.

Roentgen therapy in 1/8 unit skin doses was given in 7 cases with a temporary improvement in 3. One patient had a remission for three months following roentgen therapy of the lesions on the abdomen.

In 1 case mechanical fever therapy was given. The temperature was maintained at 104 F. for one hour. There was no improvement.

SUMMARY OF RESULTS OF TREATMENT

Of the 77 patients in this series, 54 (70.1 per cent died and 23 (29.8 per cent) were discharged from the hospital. Of the 23 patients who left the hospital, 6 were discharged as cured (3 of these had questionable diagnoses), 8 were improved and in 9 the condition was worse or unchanged. One patient, who had received germanin, sulfanilamide, sodium thiosulfate and liver extract, was seen one year after discharge and was still free of any lesions. An unsuccessful attempt was made to follow up the other discharged patients in this series; therefore, we are unable to report the end results.

SUMMARY AND CONCLUSIONS

The cause of pemphigus is still unknown.

In this series of 77 patients, 72.7 per cent were Jews and 27.2 per cent gentiles. Five and one-tenth per cent were white gentile Americans of one generation. Since most of the patients came from southeastern Europe, a geographic factor should be considered.

Laboratory investigations revealed no significant information. Postmortem examination in 11 of the cases gave essentially negative results.

While various therapeutic procedures caused temporary improvement in some cases and a disappearance of the lesions in others, the treatment of pemphigus thus far must be considered empiric.

Pemphigus is a fatal disease in most cases. Cases in which typical lesions of pemphigus have been apparently cured or in which there have been complete remissions for many years are considered by most observers to be questionable cases of this disease.

Dr. Winston Sargent of the house staff and Miss Marie Masterson and the staff of the record room of the New York City Hospital gave valuable assistance in compiling the records of these patients.

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POIKILODERMA CONGENITALE

REPORT OF A CASE IN AMERICA

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Thomson,[1] of England, in his original report described 3 patients with a condition which he named poikiloderma congenitale. The changes in the skin were present at birth and were similar to those found in poikiloderma atrophicans vasculare as described by Jacobi. Thomson called attention to the presence of developmental changes in bones, besides the abnormal condition of the skin, in each of his patients.

Chiale,[2] of the University of Milan, reported a fourth instance of the disease. In his case developmental defects of bone were not reported.

REPORT OF CASE

B. M., a white girl aged 6 years, entered the Grady Hospital in 1933, where she remained for three months. Dermatologic consultation was not requested during this period.

The following history was obtained from the mother at that time: The child was premature, weighing 4 pounds (1,814 Gm.) at birth. The delivery was normal. The mother said that "at birth the child looked like a little monkey." The skin was pitted, crinkly and rough. The nails were greatly thickened but appeared normal in size and shape.

A few days after the child's birth a red spot was noticed under her chin. When she was 3 months of age red spots appeared on the elbows and soon after were seen on the left side of the chest, the right hip and the right leg. Hair was absent at birth but began to appear at about 16 months of age. Mental development was normal. Eruption of the teeth was late; some of the baby

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1. Thomson, M. S.: Poikiloderma Congenitale, Brit. J. Dermat. **48**:221-234 (May) 1936.

2. Chiale, G. L.: Sul "Poikiloderma Congenito" del Thomson, Gior. ital. di dermat. e sif. **78**:34-55 (Feb.) 1937.

teeth never appeared. When the child was an infant the mother noticed that the right half of the body looked smaller than the left.

Between the child's second and fourth years brownish discolorations appeared on the skin. These developed, according to the mother, within "slick areas" of

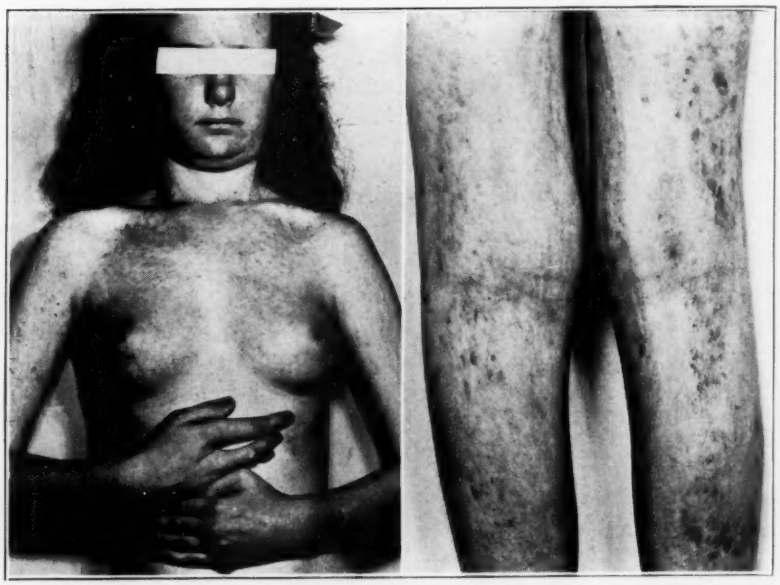

Fig. 1.—Patient with poikiloderma congenitale, showing distribution of telangiectasia and pigmentation, deformity of the right hand and bands of atrophy and areas of pigmentation on the legs.

Fig. 2.—Patient with poikiloderma congenitale, showing defective teeth and loose skin of the neck.

the skin and not on the "red areas." Menstruation began at 12 years of age. There was no history of consanguinity.

In May 1940, at the age of 13, the patient reentered the hospital. Dermatologic consultation was then requested. Asymmetry of the face and of the body was

Fig. 3.—Roentgenogram showing cystic changes in the right ileum.

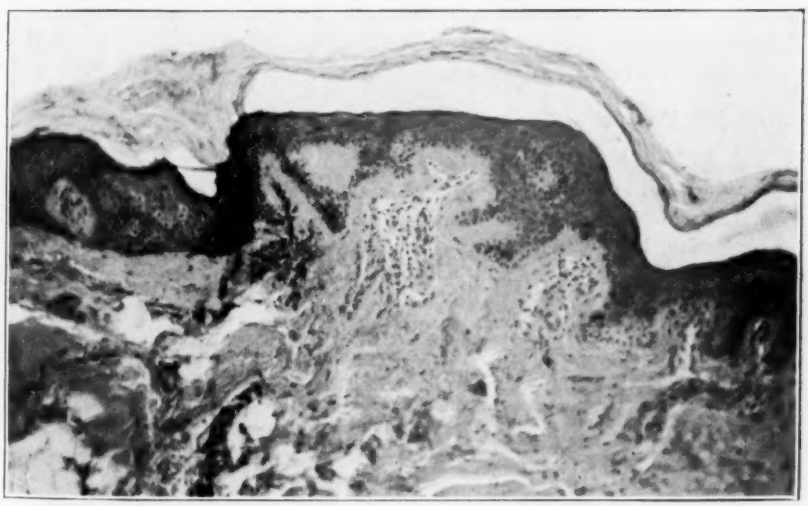

Fig. 4.—Essential histologic changes of poikiloderma congenitale, as described by Thomson.

prominent. The skin was soft and loose, and extensive telangiectasia was present. Atrophy of the skin was noticeable and appeared as pits on the face and on the body, whereas on the extremities there was a tendency toward linear arrangement of the atrophy. There was a great deal of pigmentation, especially about the atrophic areas. The teeth were defective in shape and size, and some had never erupted. Dental caries was present. The nails were greatly thickened but appeared normal in size and shape. The right hand was deformed, only three fingers being present; they were the thumb, index finger and a third finger, with a small budding rudimentary digit projecting from the distal phalanx. The blood count was normal. The blood calcium was 9.2 mg. and the phosphorus 3.2 mg. per hundred cubic centimeters. The Kahn reaction of the blood was negative.

A roentgenogram was made in the outpatient department on Aug. 24, 1939. Examination of the pelvis, the sacrum and both hip joints revealed cystic areas of bone destruction throughout the wing of the right ileum adjacent to the sacrum. Alternate areas of increased density indicated sclerosis. No sequestrums were evident. There was a deformity of the pelvis with scoliosis of the lumbar portion of the spine and sacrum with the convexity to the right. A diagnosis of low grade osteomyelitis was made.

A roentgenogram of the skull on March 23, 1940 showed no pathologic changes. Repeated examinations of the hip and pelvis were made. The last examination, on Oct. 14, 1940, revealed the same changes as the earlier ones.

Histologic examination of the skin showed the essential characteristics as pointed out by Thomson, namely, hyperkeratosis, acanthosis, atrophy, loss of papillae and confusion of the epidermodermal boundary.

SUMMARY

This case as far as we know is the fifth one of poikiloderma congenitale to be reported and the first one to be reported in America. Our patient had the characteristics of the disease described by Thomson. In addition, our patient showed an anomaly of the right hand, failure of some of the teeth to erupt and developmental defects of the other teeth.

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ABSTRACT OF DISCUSSION

DR. HAROLD N. COLE, Cleveland: I think the condition in the case presented by Drs. Hailey, Hailey and Clemens could be put in the same category with congenital ectodermal dysplasia, which Drs. Driver, Giffen, Norris, Stroud and I reported on.

Deutsch reported such a case in which the patient had a cleft hand. Cockayne mentioned this report in his book. I was unable to get the reference, but that case would be similar to the one just presented. Moreover, the patient has the same type of diffuse, disseminated atrophoderma with linear telangiectases and pigmentation. I think it is remarkable that 2 patients from different parts of the country but with almost identical conditions should be presented on the same day.

ACANTHOSIS NIGRICANS OVERLYING METASTATIC MALIGNANT GROWTHS OF THE SKIN

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Since 1890, when acanthosis nigricans was first described independently by Pollitzer [1] and by Janovsky,[2] about 300 cases have been reported. In no instance heretofore, however, has it been described in association with and immediately overlying deep metastatic malignant growths of the skin. This is different from the associated tumors, which will be mentioned later.

The cause of acanthosis nigricans is unknown. In 1895 Darier,[3] reporting his third case of the disease, associated with gastric carcinoma, advanced the hypothesis that the cutaneous change was the result of the effect of the malignant growth on the abdominal sympathetic nerves. This mechaniconervous theory was supported by Pollitzer,[4] even in regard to the benign, or juvenile form; in this type he speculated that there was some congenital abnormality, such as a fibrous band or benign tumor, interfering up to a certain point with the sympathetic function. In the various case reports and surveys of juvenile acanthosis nigricans, numerous theoretic etiologic factors, principally abnormal function of one or more of the endocrine glands, have been proposed (Wieder; [5] Knowles, Sidlick and Ludy; [6] Smith; [7] Goodman and Barthel; [8] Curth,[9] and Orol Arias and Landabure [10]).

This research was partly supported by a grant from the American Dermatological Association.

The histologic sections are filed at the Army Medical Museum, Washington, D.C., accession No. 72871.

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From the Laboratory of Dermatologic Research, University of Pennsylvania School of Medicine, and from the Philadelphia General Hospital.

1. Pollitzer, S., in Unna, P. G.; Morris, M.; Duhring, L. A., and Leloir, H.: International Atlas of Rare Skin Diseases, Leipzig, Leopold Voss, 1890, plate 10.
2. Janovsky, V., in Unna, P. G.; Morris, M.; Duhring, L. A., and Leloir, H.: International Atlas of Rare Skin Diseases, Leipzig, Leopold Voss, 1890, plate 11.
3. Darier, J.: Sur un nouveau cas de dystrophie papillaire et pigmentaire, Ann. de dermat. et syph. **6**:97, 1895.
4. Pollitzer, S.: Acanthosis Nigricans, J. A. M. A. **53**:1369 (Oct. 23) 1909.
5. Wieder, L. M.: Acanthosis Nigricans, J. A. M. A. **87**:1964 (Dec. 11) 1926.
6. Knowles, F. C.; Sidlick, D. M., and Ludy, J. B.: Acanthosis Nigricans: Adult and Juvenile Types, Arch. Dermat. & Syph. **19**:391 (March) 1929.

(Footnotes continued on next page)

In discussing the adult type of acanthosis nigricans, Masson and Montgomery [11] claimed that 80 per cent of patients who are more than 40 years of age when the cutaneous changes begin have a malignant neoplasm of the abdomen, either primary or metastatic, and that the malignant condition involves the chromaffin system and the abdominal sympathetic system by direct extension, by metastasis, by pressure or possibly by secondary toxemic changes. The other 20 per cent of the patients are those with extra-abdominal malignant growths with (1) no demonstrable intra-abdominal metastasis (Petrini de Galatz [12]), (2) no malignant process anywhere in the body (Burgess [13] and Grace and Schwartz [14]), just as in the juvenile form, and (3) such rare conditions as injury to the periadrenal tissue suffered during decapsulation of the kidney (Wise [15]).

REPORT OF A CASE

History.—A. F., a white woman aged 70, a widow, was admitted to the medical service of Dr. David W. Kramer at the Philadelphia General Hospital on Dec. 15, 1940, complaining of weakness, loss of weight and generalized itching. She was in her usual state of good health until January 1940, when she suffered for four days from nausea and pain in the upper right quadrant of the abdomen. A diagnosis of disease of the gallbladder was made. She had no further complaints until July 1940, when she noted generalized and constant pruritus. Her neighbors told her that she had jaundice, because her skin had become definitely pigmented. Both the pruritus and the pigmentation increased in the five months between the time of onset and that of hospitalization; in this period she lost 40 pounds in weight (18 Kg.) and became weak.

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7. Smith, S. W.: A Case of Juvenile Acanthosis Nigricans, Brit. J. Dermat. **45**:142 (April) 1933.

8. Goodman, H., and Barthel, E.: Acanthosis Nigricans Juvenilis: Review of Recent Literature and Report of a Case, Urol. & Cutan. Rev. **39**:487 (July) 1935.

9. Curth, H. O.: Benign Type of Acanthosis Nigricans, Arch. Dermat. & Syph. **34**:353 (Sept.) 1936.

10. Orol Arias, C., and Landabure, P. B.: Contribución al estudio de la acantosis nigricans, Rev. Asoc. méd. argent. **49**:1917 (Dec.) 1935; Acantosis nigricans. Nueva contribución a su estudio, ibid. **50**:208 (Feb.) 1936.

11. Masson, J. C., and Montgomery, H.: The Relationship of Acanthosis Nigricans to Pelvic Malignancy, Proc. Staff Meet., Mayo Clin. **11**:113 (Feb. 19) 1936.

12. Petrini de Galatz: Contribution à l'étude clinique et histopathologique de la dystrophie papillaire et pigmentaire (acanthosis nigricans) associée à un cancer pulmonaire, Ann. de dermat. et syph. **5**:321, 1914.

13. Burgess, N.: A Case of Acanthosis Nigricans, Brit. J. Dermat. **43**:169 (April) 1931.

14. Grace, A. W., and Schwartz, H. J.: Acanthosis Nigricans, Arch. Dermat. & Syph. **29**:691 (May) 1934.

15. Wise, F.: Acanthosis Nigricans Following Decapsulation of the Kidneys, J. Cutan. Dis. **36**:35 (Jan.) 1918.

No symptoms referable to the cardiovascular and respiratory systems could be elicited. She had slight anorexia but no nausea or emesis; gaseous eructations were troublesome but were relieved by simple alkali. No abnormality of the character or habit of the stool were noted. She had nocturia for five years, but there was no change in the color of the urine.

The family history contained no instances of metabolic disease or of malignant growth.

Physical Examination.—The patient was emaciated and weak and was constantly scratching her abdomen and breasts. The temperature (rectal) was 100.4 F., the pulse rate 88 a minute, the respiratory rate 20 a minute and the blood pressure 136 mm. of mercury systolic and 76 mm. of mercury diastolic. The skin exhibited a diffuse dark yellowish brown pigmentation, which was most prominent on the face, retroauricular areas, neck, axillas, anterior parts of the chest and perineum. In the perineal and axillary zones the skin was roughened, thickened and verrucous. Many linear excoriations and pinhead-sized bloody crusts were present on the shoulders, abdomen and thighs, but no parasites were found. The lymph nodes in the left supraclavicular and left axillary and both inguinal regions were enlarged, moderately firm, nontender and somewhat matted together but movable. The scleras were white. The mucous membrane of the eyes, nose, mouth and throat showed no abnormal pigmentation. The tongue was dry, and, except for two teeth, the patient was edentulous. The percussion note over the base of the right lung posteriorly was impaired. Otherwise the lungs were clear and resonant. The heart was normal. The abdomen protruded prominently but was not tender, and each flank bulged. A mass filling the epigastrium and extending 1 cm. below the umbilicus was palpable to the left of a questionably enlarged liver. The spleen was not felt. Bimanual pelvic examination was not satisfactory, but the vaginal mucosa showed no abnormal pigmentation. Digital rectal examination gave normal results. The only skeletal abnormality was a moderate dorsal kyphosis. The extremities were thin, with normal arterial pulsations and deep tendon reflexes within physiologic limits.

Laboratory Studies.—The Kahn reaction of the blood was negative. A blood count revealed 3,450,000 erythrocytes and 6,000 leukocytes per cubic millimeter. The stained blood film showed 81 per cent neutrophils, 16 per cent lymphocytes, 1 per cent monocytes and 2 per cent eosinophils. There was 9.5 Gm. of hemoglobin per hundred cubic centimeters (Haden Hausser hemoglobinometer). Chemical analysis of the blood showed the following results: 87 mg. of blood sugar per hundred cubic centimeters; 35 mg. of urea nitrogen; 216 mg. of serum cholesterol (Reinhold method), with a normal range from 100 to 350 mg.; 96 mg. of cholesterol esters, or 45 per cent of serum cholesterol (Reinhold method), with a normal range from 50 to 80 per cent of total cholesterol, and 615 mg. of serum chloride (as sodium chloride [Van Slyke method]). The icterus index was 7.

A roentgenogram of the chest disclosed only increased prominence of the lower trunk shadows on the right side, and on an abdominal survey film cholelithiasis was demonstrable.

Hospital Course.—With a low grade fever and no response to symptomatic therapy, the patient rapidly became more and more cachectic and died on December 24.

Necropsy.—The necropsy was performed eighteen hours after death by Dr. Benjamin Gouley.

External Examination.—The body showed extreme emaciation but no cyanosis or edema. A diffuse generalized brown pigmentation was present, most prominent

in the perineum and axillas and on the neck and chest. The anogenital and, less so, the axillary skin was verrucous. The lips and oral mucous membrane exhibited no definite pigmentation. The scleras were free from icterus and other discoloration. Enlarged lymph nodes were palpable cephalad to the mesial end of the left clavicle and in each inguinal region. The breasts were of equal size and free from nodules.

Internal Examination: The pleural surfaces were smooth and glistening. The right pleural sac contained 800 cc. of clear pale yellow fluid.

The pericardial surfaces showed no significant changes and enclosed the usual amount of clear amber fluid.

There was no free fluid in the peritoneal cavity. The parietal peritoneum was infiltrated in many places by soft grayish white nodules; in the mesentery and omentum there were similar masses and enlarged lymph nodes. The latter were soft, on section gray and white, and not hemorrhagic; they were discrete, although forming compact masses. The periaortic, peripancreatic, hypogastric and iliac lymph nodes showed the same changes. This tissue formed a rounded retroperitoneal mass, measuring about 12 cm. in diameter, which surrounded both kidneys, encasing especially the left kidney and the left adrenal gland.

Aorta: The caliber was normal and not impinged on by the enlarged periaortic masses. The intima was smooth and gray.

Heart: The organ was of normal size and contour. The myocardium was uniformly reddish brown. The endocardium and valves were not thickened. The upper portion of the interatrial septum contained a nodular infiltration of gray tumor tissue, measuring 1.5 cm. in diameter. The coronary arteries were patent, of normal caliber and free from atheroma.

Lung: The consistency of both lungs was moderately and uniformly increased. Blood-tinged frothy fluid escaped from the cut surfaces when pressure was made on the lung parenchyma. The bronchial mucosa was hyperemic. The pulmonary vessels contained no thrombi. The regional lymph nodes were large and soft, and one node invaded the left main stem bronchus, elevating but not eroding the bronchial mucosa.

Spleen: The spleen weighed 110 Gm. and was slightly enlarged and extremely soft. The capsule was thin, smooth and slate gray. The pulp was pale grayish red, and the markings were indistinct.

Kidneys: The left kidney was slightly enlarged and flaccid. On section the parenchyma was found to be much diminished, the cortex measuring 2 to 3 mm. The pelvis was widely dilated, and the pelvic mucosa was thin and gray. Neoplastic tissue was found infiltrating the wall of the proximal portion of the left ureter and almost occluding the lumen. The right kidney was normal in size, with average consistency and corticomedullary ratio. The pelvis and ureter showed no change.

Urinary bladder: The wall was not thickened; the mucosa was thin and gray. Trabeculation was of usual prominence.

Genitalia: Each broad ligament was so thickened by an infiltration of neoplastic tissue that neither uterine tubes nor ovaries could be identified. The uterus was small and firm.

Gastrointestinal tract: The esophageal lumen was of average size. The stomach was moderately dilated; the wall was of usual thickness, but the rugae were flattened. Three circular ulcers, varying from 1.5 to 4 cm. in diameter, were rather closely situated on the greater curvature, about midway between the cardia and the pylorus. The base of each ulcer was free from hemorrhage and hyperemia and was ridged by firm yellow white tissue, which also formed the edges of the

ulcers. Irregular sheetlike infiltrations of white tumor tissue lay on the serosal aspect of these lesions. The pylorus appeared normal. The duodenum contained a currant jelly-colored collection of partially digested blood and mucus which increased in quantity throughout the small bowel downward to the ileocecal junction. The mucosal and serosal surfaces of the small and large intestine were intact and essentially normal in appearance. The mesenteric blood vessels showed no change.

Liver: This organ weighed 1,710 Gm. and was slightly enlarged and moderately soft. The capsule was thin and translucent. Resistance to cutting was slightly diminished; the cut surface was pale reddish brown and soft, and the markings were obscured.

Gallbladder and Bile Ducts: The gallbladder was of normal size, but the wall was slightly thickened. The mucosa was reticulated. Numerous small, soft, greenish white calculi occupied the lumen. The bile ducts were patent, not dilated and free of calculi.

Pancreas: The organ was surrounded by lymph nodes that were a seat of neoplastic change. These infiltrated the head of the pancreas but involved neither the pancreatic nor the common bile ducts.

Adrenals: The left adrenal was buried deep in the large retroperitoneal mass. When the latter was sectioned, the neoplastic tissue on the cut surface bulged over and almost obscured the adrenal parenchyma. The gland was of usual length, but it was definitely compressed and showed a narrow dark brown cortex. Although embedded in tumor tissue, the right adrenal was not compressed; its cortex was more distinct but did not show the usual yellow color.

Thyroid: This gland was small and uniform in consistency and color.

Pituitary: The pituitary gland was smaller than normal, and in the anterior lobe there was a small nodule which on histologic examination was shown to be an area of necrosis instead of tumor tissue.

Skeleton: The body of the first lumbar vertebra and the dorsal segments of the tenth and eleventh ribs on the left side were softened, and on section the cut surfaces showed soft white tissue replacing the normal osseous structure. Elevating the periosteum on the ventral aspect of the manubrium there was a nodule of similar tissue.

Brain and meninges: Excepting hyperemia of the meningeal vessels, there were no noteworthy changes.

Histologic Examination.—All the sections of the retroperitoneal tumor showed a dense cellular growth consisting of large cells, mostly round, with large, prominent basophilic nuclei, frequently multinuclear. There were occasional large giant cells containing five or six nuclei. The tumor cells were densely packed, appearing occasionally in what seemed to be rows or else in sheets but most often in a solid mass without any definite grouping. Very little stroma was present, and thin-walled vascular spaces were fairly numerous. The histologic diagnosis was lymphosarcoma. An identical picture was seen in the involved lymph nodes, the periadrenal tissue, the bases of the gastric ulcers, the involved bones and the nodule in the heart.

The adrenal tissue was completely surrounded by dense neoplastic tissue (figs. 1 and 2). There was apparently partial atrophy of the gland, involving particularly the midzone (zona fasciculata). In many fields the cellular columns were broken down and in varying states of disintegration. The medulla was not included in the sections.

The skin from the perineal region (Laboratory of Dermatological Research, University of Pennsylvania, accession number 3789) showed an epidermis with

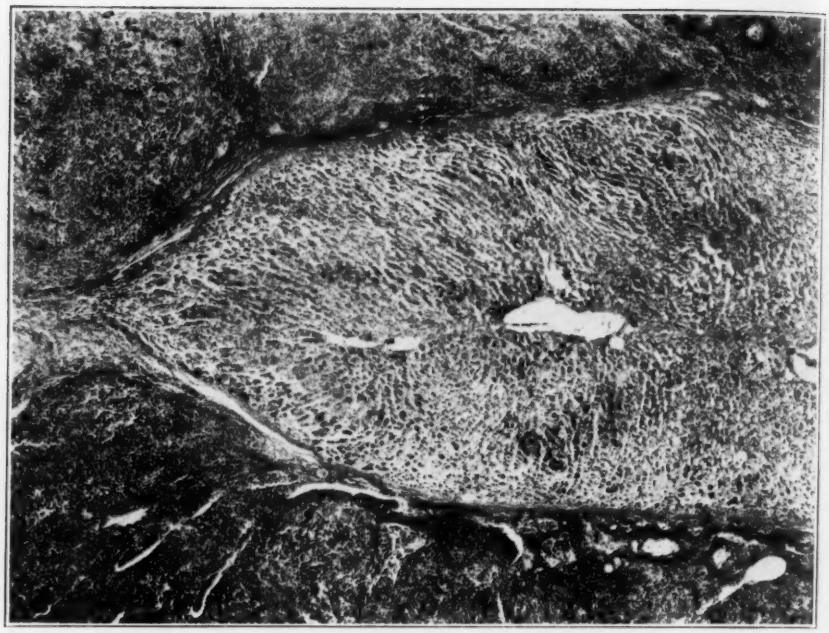

Fig. 1.—Adrenal surrounded by mass of tumor (hematoxylin and eosin, × 18).

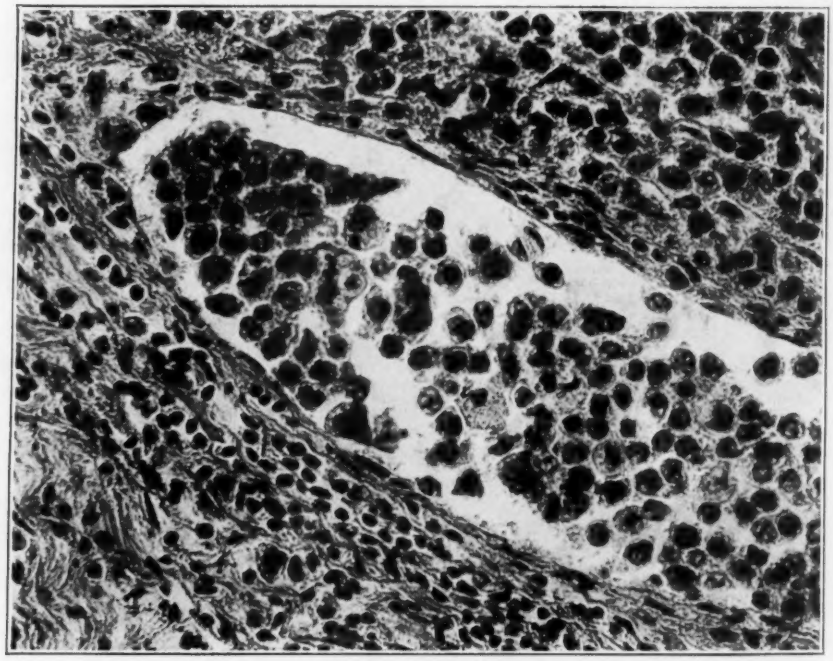

Fig. 2.—Capsule of adrenal in lower left hand corner and tumor mass at upper right; mass of tumor cells in an endothelial-lined space, probably lymphatic (hematoxylin and eosin, × 307).

definite irregularities due to closely placed low verrucous elevations. There were relative and absolute hyperkeratosis and evidence of atrophy of the prickle cell layer with adjacent areas of acanthosis. The pigment content of the basal cells was notably increased. In the corium the collagenous bundles were loosely arranged, as in edema, but there were not any associated inflammatory phenomena. These changes were typical of those described as diagnostic by Montgomery and O'Leary.[16] The dilatation of some sweat ducts was great enough to suggest syringoma, but the presence of secretory coils in the subcutaneous fat justified dismissal of this diagnosis. Extending diffusely and widely in the deeper parts of the corium and in the subcutaneous fat, there were many of the

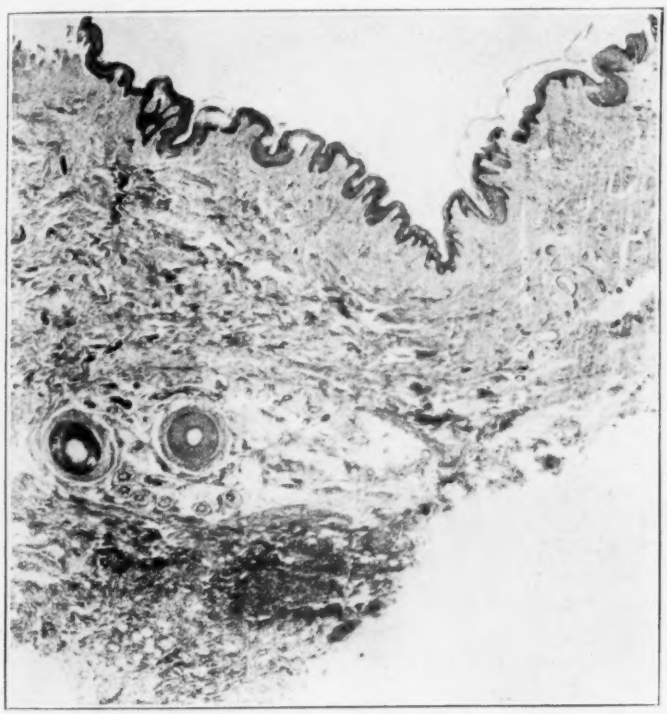

Fig. 3.—Photomicrograph of skin (hematoxylin and eosin, × 20). Papillary features of acanthosis nigricans at the surface and tumor metastasis (darkly staining) at the bottom of the section, with a group of dilated sweat ducts showing faintly at the extreme right.

large round tumor cells already described (figs. 3 and 4). The histologic diagnosis of the perineal skin was acanthosis nigricans[17] and metastatic cutaneous and subcutaneous lymphosarcoma.

16. Montgomery, H., and O'Leary, P. A.: Pigmentation of the Skin in Addison's Disease, Acanthosis Nigricans, and Hemochromatosis, Arch. Dermat. & Syph. **21**:910 (June) 1930.

17. Histologic diagnosis confirmed by Hamilton Montgomery, M.D., Mayo Clinic.

CUTANEOUS TUMORS ASSOCIATED WITH ACANTHOSIS NIGRICANS

Gates [18] found in an autopsy series of 2,298 patients with malignant tumors of various types, including leukoses, that 2.7 per cent had metastasis to the skin and clearly demonstrated the fact that a tumor which produces extensive metastasis in internal organs is one most likely to metastasize to the skin. In other words, the skin largely escapes metastasis except in a case in which the neoplasm is a widely metastasizing one. Of a total of 442 cases of cutaneous metastasis (Gates reported 93 cases and collected 349 from the literature), the malignant tumor was

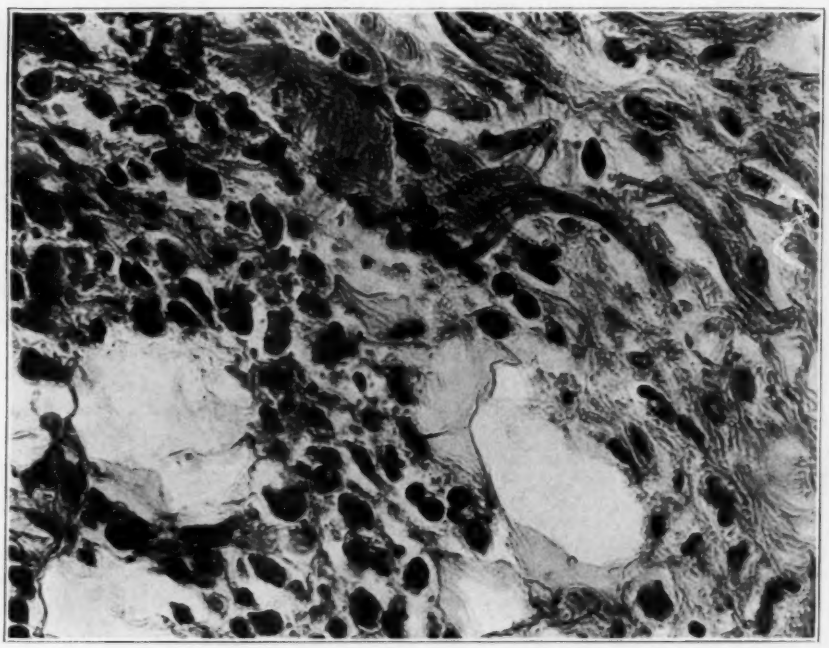

Fig. 4.—Photomicrograph of the skin (hematoxylin and eosin, × 307). Metastatic tumor cells at the junction of the corium and subcutaneous fat.

classified as lymphoma in 91 cases, but in only 7 instances was the primary growth a sarcoma. This survey did not include subcutaneous metastases, such as those in the case of retroperitoneal lymphosarcoma reported by Matheson,[19] in which numerous discrete painless subcutaneous growths developed, varying in size from miliary dimensions to those of a cherry. Recently Bingham and Quarrier [20] reported a case

18. Gates, O.: Cutaneous Metastases of Malignant Disease, Am. J. Cancer **30**:718 (Aug.) 1937.

19. Matheson, N. M.: Multiple Subcutaneous Nodules in a Case of Lymphosarcoma, Brit. J. Dermat. **47**:233 (June) 1935.

20. Bingham, C. T., and Quarrier, S. S.: Reticulum Cell Sarcoma, Arch. Dermat. & Syph. **41**:722 (April) 1940.

of reticulum cell sarcoma with multiple intracutaneous nodules, but acanthosis nigricans was not associated in this case or in the aforementioned sarcomas and lymphomas.

It appears that in only 3 instances of acanthosis nigricans have cutaneous tumors been reported. In each of them the relation of the tumor to the production of acanthosis nigricans was different. The tumor may be considered as the initiating process, as in the case of leiomyosarcoma cutis reported by Schlammadinger;[21] in this case the photomicrographs showed an atrophic epidermis overlying the neoplasm and no tumor in the section of acanthosis nigricans, which clinically was localized near it. On the other hand, the cutaneous neoplasm may be unrelated, as was the incidental trichoepithelioma found by Dowling and Freudenthal[22] in the histologic section taken from a patient with acanthosis nigricans and presumable but not proved gastric carcinoma. Similarly, a case of acanthosis nigricans in a dog was reported by Curth and Slanetz,[23] two subcutaneous nodules having been proved at autopsy to be lipomas and in no way related to the probable primary adenocarcinoma of the liver.

COMMENT

How shall one correlate the facts and interpret the findings detailed in the history of the patient reported here? May the changes in the superficial part of the skin be ascribed to the deep cutaneous metastases? By and large, such a conclusion seems unwarranted and illogical, since a similar combination of dermatoses was not found in the axillary skin. Likewise, this view is not applicable to benign acanthosis nigricans or to acanthosis nigricans in adults who do not have any malignant growths. Nor would it explain instances, such as Masson and Montgomery[11] reported, in which the acanthosis nigricans was present for ten years before any symptoms attributable to abdominal neoplasm developed or Freund's[24] case of adenocarcinoma of the breast developing sixteen years after the onset of the acanthosis nigricans. Nonetheless, one must remember that with few exceptions the photomicrographs of acanthosis nigricans in the literature include only the epidermis and the most superficial portion of the corium. Most of the specimens taken were for biopsy and not at necropsy, as in my case. Accordingly, it is conceiv-

21. Schlammadinger, J.: Leiomyosarcoma cutis mit Acanthosis nigricans vergesellschaftet, Dermat. Wchnschr. **99**: 1257 (Sept. 29) 1934.

22. Dowling, G. B., and Freudenthal, W.: Acanthosis Nigricans, Proc. Roy. Soc. Med. **31**:1147 (July) 1938.

23. Curth, H. O., and Slanetz, C. A.: Acanthosis Nigricans and Cancer of the Liver in a Dog, Am. J. Cancer **37**:216 (Oct.) 1939.

24. Freund, E.: Cas d'acanthosis nigricans. Apparition d'un carcinome après seize années, Rev. franç. de dermat. et de vénéréol. **7**:450 (Sept.) 1931.

able that study of the pars reticularis and subcutis in other cases of this condition would have revealed associated metastases in the deep parts of the skin.

Is one justified, then, in assuming that the dermatosis is a manifestation directly related to some disturbance of function in the abdominal cavity provoked by the lymphosarcoma? This view is more plausible, since the condition conforms readily to Darier's mechaniconervous theory, with both the adrenal and the abdominal sympathetic system involved by the primary or secondary growths.

The pruritus in this patient has been disturbing because it is not a symptom of acanthosis nigricans,[4] nor is it caused by secondary deep malignant growth in the skin.[25] In this case the pruritus was universal and began almost simultaneously with the generalized pigmentation. It would be logical, therefore, to ascribe a common cause for both the melanization and the pruritus, such as the products of the cachexia due to neoplasm, rather than to consider the pruritus due to incidental disease factors, such as retention of nitrogenous products in uremia, parasitic infestation or senile changes.

SUMMARY AND CONCLUSION

A case of acanthosis nigricans is reported in which deep cutaneous and subcutaneous metastases from a retroperitoneal lymphosarcoma were observed histologically. The etiologic relation is discussed. It may be advisable to include the deepest parts of the corium and subcutaneous fat in future histologic examinations in cases of acanthosis nigricans.

Dr. Fred D. Weidman gave valuable assistance, with time, material and knowledge.

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25. Eller, J. J.: Tumors of the Skin, Philadelphia, Lea & Febiger, 1939, pp. 290-292.

BULLOUS DYSKERATOSIS OF THE KERATOSIS FOLLICULARIS (DARIER) TYPE

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AND
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In the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY of March 1939 we [1] described, under the designation of keratosis follicularis (Darier) with vesiculation, an unusual clinical picture of a patient. One month later in the same journal Hailey and Hailey [2] reported 4 cases, those of two pairs of brothers, of an eruption which corresponded suggestively to the condition in our case. They viewed the disease as a hitherto undescribed one and designated it familial benign chronic pemphigus. In September 1939 Ayres and Anderson [3] reported under the title "Recurrent Herpetiform Dermatitis Repens" 5 cases of a vesicular and bullous eruption which they admitted was identical with that in the cases described by Hailey and Hailey. Since that time Hailey and Hailey [4] have published another series of familial cases of the disease and again expressed the opinion that the dermatosis represents a form of pemphigus and a new dermatologic entity.

We have had access to some of the histologic specimens of the lesions of the 4 patients of Hailey and Hailey, and the microscopic picture corresponds with that of our patient. Our patient is still under observation, and he has volunteered the information that he now recalls clearly and with certainty that his paternal grandmother and uncle, his father and one of his three brothers (a total of 5, including our patient) had an

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1. Pels, I. R., and Goodman, M. H.: Criteria for the Histologic Diagnosis of Keratosis Follicularis (Darier): Report of a Case with Vesiculation, Arch. Dermat. & Syph. **39**:438 (March) 1939.

2. Hailey, Howard, and Hailey, Hugh: Familial Benign Chronic Pemphigus, Arch. Dermat. & Syph. **39**:679 (April) 1939.

3. Ayres, S., and Anderson, N. P.: Recurrent Herpetiform Dermatitis Repens, Arch. Dermat. & Syph. **40**:402 (Sept.) 1939.

4. Hailey, Howard, and Hailey, Hugh: Familial Benign Chronic Pemphigus: Report of Thirteen Cases in Four Generations of a Family and Report of Nine Additional Cases in Four Generations of a Family, South. M. J. **33**:477 (May) 1940.

eruption for many years which was similar to his.[5] It is evident that the dermatosis of our patient is the same as that subsequently described by the various aforementioned authors.

The largest series of cases, 27 of 78 persons in three generations of the same family being afflicted, was reported before the Chicago Dermatological Society by Becker and Obermayer [6] on Nov. 15, 1939, and a discussion of the clinical and microscopic picture of a representative case appeared in the transactions of that society.

On the basis of our studies we stated the opinion that this disease is a form of dyskeratosis, and since the microscopic picture corresponds in its essentials to that of Darier's disease, we felt obliged to label the dermatosis as vesicular or bullous Darier's disease.

We are, naturally, not interested in what name is given to the disease in the cases under discussion. Our prime purpose is to review the data bearing on our case and on those reported and discussed in the literature, in order to establish the distinguishing features of the disease and thereby classify it properly. One of us (M. H. G.),[7] in correspondence in the ARCHIVES, took issue with the contention of Hailey and Hailey that the condition in their cases was of the nature of pemphigus. We believe that most of the evidence gathered from the studies of all of the cases lends confirmation to the view which we originally expressed in the first report of this peculiar disease, namely, that it represents a dyskeratosis of the nature of Darier's disease with the added feature of vesiculation. We are, incidentally, not averse to the designation suggested by Rein and Frank,[8] namely, dyskeratosis vesicularis hereditaria, since this term would aptly fit the aspects of the malady similar to Darier's disease. We are, however, opposed to the use of the terms pemphigus and pemphigoid dermatitis, because we feel there is nothing in this condition to suggest any relation to either of these inflammatory processes.

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5. We have recently encountered a typical example of this dermatosis with lesions on the neck in a 52 year old woman who stated convincingly that there was no family history of the condition. This may indicate that, as in Darier's disease, there may be sporadic, nonfamilial cases.

6. Becker, S. W., and Obermayer, M. E.: Bullous Disease: Bullous Darier's Disease (Pels and Goodman); Familial Benign Pemphigus (Hailey and Hailey); Herpetiform Dermatitis Repens (Ayers and Anderson), Arch. Dermat. & Syph. **41**:1170 (June) 1940.

7. Goodman, M. H.: Familial Benign Chronic Pemphigus, Correspondence, Arch. Dermat. & Syph. **40**:272 (Aug.) 1939.

8. Rein and Frank, cited by Wise, F., and Sulzberger, M. B.: Editorial Comment, in Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1939, p. 235.

REVIEW OF PREVIOUS OBSERVATIONS

Our case, the first of its kind to be reported, was, in brief, as follows:

E. L., a 40 year old Chinese, had an eruption which first appeared when he was 19 years of age. There were exacerbations and remissions of an essentially moist, crusting, vesciular and bullous eruption. Lesions were always present at one or more of the sites of predilection, such as the back and sides of the neck, axillas, groins, scrotum, penis, perianal region, abdomen and toe webs. There was intense itching at times not only in areas of involvement but also of the apparently normal skin. The lesions remained localized at the sites mentioned and would appear as poorly formed vesicles and bullae which tended toward rapid rupture, oozing and crust formation. It was apparent that the blister resulted from a raising up of a grayish white, thick, semitranslucent, horny membrane which covered a slightly infiltrated papular base. The crusts, which were almost constantly present, were rather delicate and thin, apparently free from any coarse elements such as epidermal products. In other words, the thick-walled epidermal membrane would rupture, and a thin milky fluid would escape, with resultant collapse of the vesicle walls. The nature of the underlying base became apparent from time to time when vesicular or bullous formation would cease and active surface changes would be suspended. The base was composed of reddish brown coalescent faint papules, most of which were angular, flat topped or truncated, though some were smoothly or irregularly rounded. When involution took place, the skin at the involved sites would be restored to normal except for brownish pigmentation. During periods of activity of the disease scratching would elicit at any area on the trunk and extremities, and occasionally on the face, tiny lesions consisting of a few grouped or coalescent, smooth, flat-topped, slightly elevated, pinhead-sized papules, usually uniformly rounded but frequently of irregular angulated outline and moderately infiltrated. The most elevated papules reached the height of 2 or 3 mm., showed a somewhat granular surface and had a glazed or a crusted scale. These papules were reddish brown to purplish red and simulated those which, as coalescent patches, always constituted the base on which bullae would form in the areas of predilection.

The question of papules in this dermatosis will again be mentioned.

At this point it should be stressed that the elicitation of isomorphic phenomena on scratching (Köbner's sign) has been observed as a characteristic in typical Darier's disease.[9] Hailey and Hailey [2] stated that a Nikolsky sign was elicited, whereas Becker and Obermayer [6] stated that in their cases a pseudo Nikolsky sign was elicited. We are inclined to agree with the latter, because the apparently normal skin in our case could not be denuded by friction. On the other hand, in involved areas the intact surface epidermal membrane could be detached with friction, and also in the adjacent skin, where there might have been impending activity, denudation could be obtained in small areas.

9. Bettmann: Ueber Umbauvorgänge als Ausdruck spezifischer Reaktionsfähigkeit bei Hautkrankheiten (Die Reizbarkeit der Haut bei der Darierschen Krankheit), Arch. f. Dermat. u. Syph. **135**:65, 1921.

In our original report we outlined the details of our histologic observations.

The microscopic picture of early and late lesions on general survey corresponded to that which is found in typical Darier's disease. There was a breaking away of the rete cells from a basal layer which usually remained intact and adherent to the corium, with the result that lacunar spaces and fissuring were in evidence. Disrupted rete cells lying free within the spaces tended to become rounded and their cytoplasm lighter pink staining, and the nuclei were pyknotic. In the upper portion of the rete the prickle cells remained normally intact but stained relatively lighter than the cells in the region of the basal layer. In sections from frank bullous lesions the superficial rete cells had undergone degeneration and were replaced by a vesicular space which occasionally was separated from the underlying lacuna by a narrow bridge of rete cells which had not yet undergone disruption. Often the two spaces would merge into one another to produce a vesicular cavity which extended from the basal layer to an intact horny layer above. The granular layer appeared occasionally to be wider than normal but actually had disappeared at other points where the disease was active. Typical *corps ronds* and *grains* were not seen in sufficient number for them to be considered characteristically present, but, on the other hand, in some sections there were present unmistakable elements of the *corps ronds* type together with a few *grains*. These elements were never seen high up in the epidermis or penetrating into the granular or horny layer, but they remained confined to the midportion of the rete among the disrupted cells about the lacunar space or in a larger bullous space. The horny layer was always found to be intact and slightly or moderately thickened. Rarely a few parakeratotic cells were present beneath the horny layer. The changes of inflammatory nature in the corium were of a banal type and apparently were of secondary significance.

ADDITIONAL STUDIES ON THE PECULIARITIES OF THE DARIER TYPE OF DYSKERATOSIS

In our original article we stressed an easily forgotten characteristic feature of the lesions of typical Darier's disease, namely, the crusting. It behooves us to mention briefly how fluid trickles through and escapes to the surface of lesions which are of keratotic structure. The keratotic papule is composed essentially of an acanthotic rete with its fluid-containing lacuna, an accentuated granular layer and a thickened horny layer. *Corps ronds* in greater or lesser numbers are present in the lower and middle portions of the rete within and adjacent to the lacuna. The transformation products (the final elements of the dyskeratosing process) of the *corps ronds,* which are *corps grains,* become scattered through the horny layer often in collected masses, referred to as keratoid masses by Darier,[10] and actually replace certain portions of this outer layer. Manifestly, then, in Darier's disease the genetic dystrophy of the basal

10. Darier, J.: Note sur l'anatomie pathologique de la maladie dite "psorospermose folliculaire végétante" à propos d'un cas nouveau, Ann. de dermat. et syph. **7**:742, 1896.

cells leads to an increased normal keratinization (hyperkeratosis), deficiency in normal keratinization (parakeratosis) and an abnormal keratinization (so-called keratoid masses). The presence of a surface layer composed of an intermixture of horny material with cells of parakeratosis and *corps grains* could explain the trickling outward of fluid from the lacunar space through a disrupted rete layer and, therefore, the crusting in typical Darier's disease (fig. 1).

Our studies of typical Darier's disease in conjunction with and in the light of those made of microscopic sections from our case and from 2 of the cases of Hailey and Hailey have led us to the conclusion that, aside from the hitherto well recognized elements of dyskeratosis, repre-

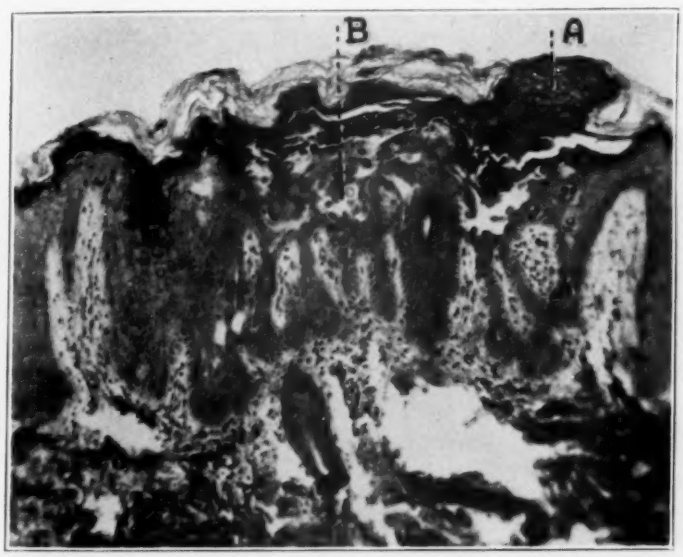

Fig. 1.—Section from a case of typical Darier's disease. *Corps ronds* (*B*) are prominent, and the hyperkeratosis is accompanied by parakeratosis and large numbers of *corps grains* (so-called keratoid mass) (*A*).

sented by *corps ronds* and *grains,* there is another feature which must be considered fundamental to the phenomenon of dyskeratinization in this disease. In our original paper, we stated the impression that one of the earliest changes in the disease is acanthosis, and we suggested that there is a hyperplasia of the basal cells. Sections from lesions of typical Darier's disease and from a biopsy specimen, consisting of a tiny linear group of connected brownish red papules appearing in a line of scratch (Köbner phenomenon) on the left wrist of our patient, serve to bear out the latter point (fig. 2). This lesion was excised within thirty-six hours after its appearance.

In specimens of early lesions and also in those of more advanced ones we have noted just above the basal layer cells which resemble closely the basal cells themselves. These cells are of the elongated (cylindric) basal type (fig. 2), with a large deeply chromatic nucleus which occupies the greater portion of the cell, surrounded by a darkly stained cytoplasm. The splitting which results in fissures and lacunas seems to take place

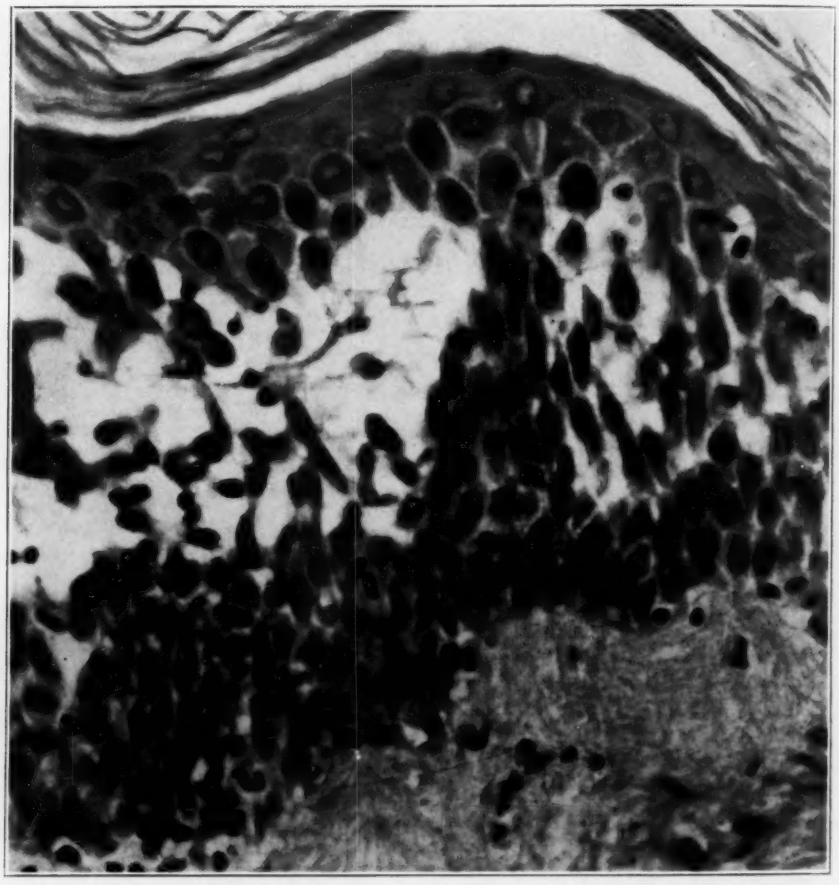

Fig. 2.—Section from a thirty-six hour old lesion. *Corps ronds* and *grains* are scarce, and parakeratosis is minimal or absent. Note the intact thickened horny layer and the apparent hyperplasia of highly chromatic cylindric cells of the basal type devoid of prickles.

between these cells or between small groups of such cells. We expressed the opinion that the pathogenesis of Darier's disease may, at least in one respect, be based on a speeding up or a slowing down of the function of the basal cells in their production of prickle cells. It is conceivable that in this process there would appear in the suprabasal position a cell which

not only approaches the basal form in appearance but which also may be devoid of spinous processes and incapable of developing keratinous features either prematurely (*corps ronds*) or normally (horny layer). In brief, from the evidence at hand, we are inclined to conclude that in Darier's disease a fundamental phenomenon of dyskeratosis is the formation of cells of the basal type which are deficient in the properties necessary to produce normal prickle cells. Brünauer [11] discussed the tendency toward hyperplasia of the basal cells in Darier's disease.

With these facts in mind we have a plausible explanation for the formation of bullae in the type of Darier's dyskeratosis represented by the condition in our case. There are few *corps ronds* and therefore an absence of *grains* to soften or to enfeeble the horny layer, and parakeratosis is at a minimum. As we have pointed out in the clinical description of the case, there is an intact, normal, thickened stratum corneum, obviously impermeable to the penetration of fluid which accumulates beneath it, as in typical Darier's disease. Under such circumstances, as this fluid accumulates and under mounting tension disrupts the rete cells, it tends to push upward the overlying cornified membrane to form a bulla which on rupture would permit its escape. It seems, then, that the character of the lesion depends on which feature of dyskeratosis predominates. In the typical Darier's dermatosis the predominating *corps ronds* and *grains* add up with other features to give a crusted hyperkeratotic lesion, whereas in the bullous form originally described by us the almost complete absence of *corps ronds* and *grains* and the predominance of the nonkeratinizing basal type of cells plus the heightened normal keratinization would lead to a bullous lesion.

In our original paper we expressed the opinion that the phenomenon of fissuring or lacunar formation was the most important criterion in the diagnosis of Darier's disease. In a study of many sections from cases of typical Darier's disease and from the case under discussion, we have consistently noted that the "roof" and the bottom layer of the characteristic areas of separation apparently would, if approximated, fit into one another almost perfectly. We therefore felt that in the Darier type of dyskeratosis there takes place, in conformity with our previous explanation, an interruption or spacing because of the absence of prickles in the hyperplastic basal cells or the loss of them in the prematurely keratinizing cells (*corps ronds*). We attempted to prove that in vivo there is only interruption or potential separation and that the actual fissuring and fully developed lacunas seen in stained sections are a consequence of excision and manipulation of the block of tissue and of the processes of fixing, dehydrating and staining. A biopsy specimen taken from the papular area (fig. 3) of our patient was placed in salt solution

11. Brünauer, S. R.: Morbus Darier, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 8, pt. 2, pp. 244, 254 and 258.

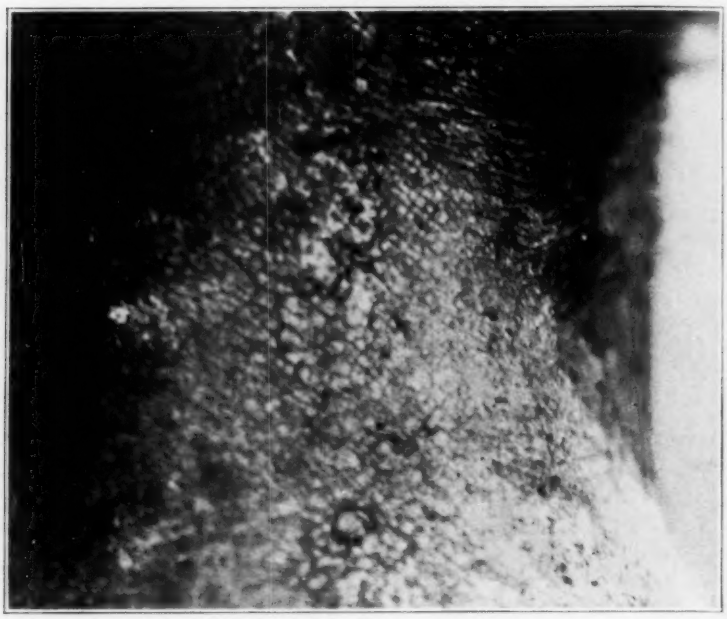

Fig. 3.—A papular area on the back of the neck photographed when vesiculobullous formation was in abeyance.

Fig. 4.—Serial section of the papular area shown in figure 3, hardened and cut with the freezing microtome. Note the minor fissuration as compared with that in figure 5.

for a few minutes, and then a number of serial sections were cut with the freezing microtome and stained with hematoxylin and eosin. The remainder of the block was treated in the routine manner, with fixation in solution of formaldehyde and the alcohols and staining with hematoxylin and eosin. It can be noted in the photomicrographs (figs. 4 and 5) that our impression is apparently confirmed, since the sections from the block which had sustained only the manipulation incidental to excision and freezing showed only slight fissuring here and there in the

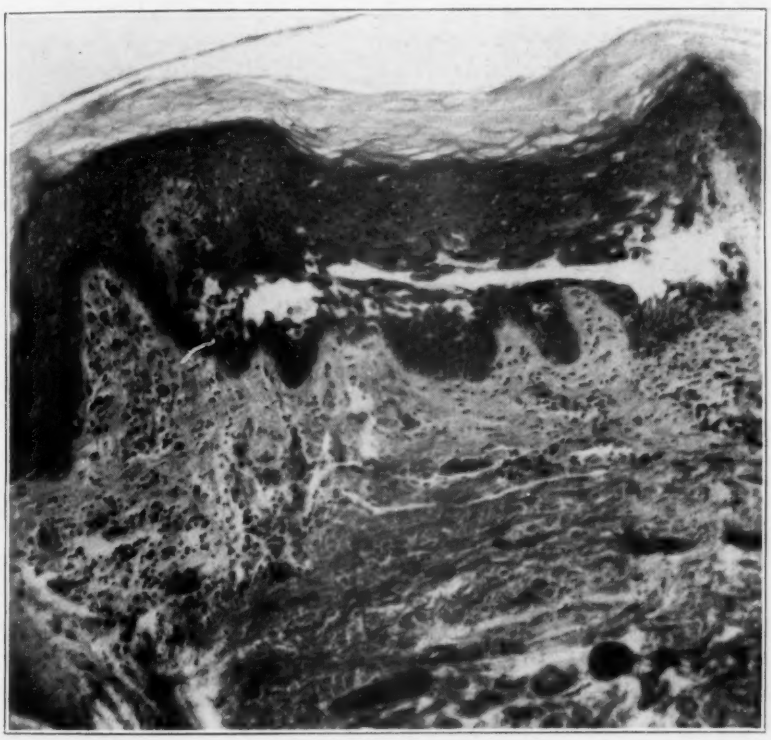

Fig. 5.—Serial section from the same tissue block as that in figure 4. Note the typical fully developed fissures and lacunas apparently resulting from the routine manipulation, fixation, dehydration, sectioning and staining of the remaining portion of the biopsy specimen.

rete layer, whereas the sections from the portion of the same block which had undergone the entire routine from fixation to staining showed the typical fully developed fissures and large lacunas.

EVIDENCE FAVORING A FORM OF DARIER'S DYSKERATOSIS

Two of the 4 cases included in the first report of Hailey and Hailey were those of brothers who had been originally examined by Dr. J.

Richard Allison. Histologic sections from these cases were said to show dyskeratosis, and a "group of dermatologists" considered them to show Darier's disease.

Weidman, in his discussion of our original communication,[1] expressed doubt that the condition in our case represented a form of Darier's disease. He stated that "there are so few clinical observations which suggest Darier's disease that the histologic changes alone should not be regarded as diagnostic."

In the aforementioned correspondence of one of us (M. H. G.),[7] the points in favor of a form of Darier's dyskeratosis included the distribution of the eruption in seborrheic areas. We must add that our patient from time to time showed typical lesions on the face, particularly on the chin and behind the ears, and there was occasional evidence of the disease in scratched areas on the scalp. The age of onset in the 27 familial cases, the details of which were presented by Becker and Obermayer, was 16 to 18 years. In all of the other cases reported, including our own, the eruption developed first in this general age period. This feature conforms with the usual time of onset of Darier's disease.

Montgomery,[12] in discussing the cases of Becker and Obermayer, stated that sections from these cases showed *corps ronds, grains* and *Lücken*, or spaces characteristic of Darier's disease, whereas the histologic changes in the cases reported by Hailey and Hailey suggested pemphigus but failed to show the features of Darier's disease. He concluded that "both types of histologic change may be seen in these cases, which together with the clinical history and familial incidence make this condition distinct from either ordinary pemphigus or Darier's disease." We cannot agree with this interpretation, because there are in the clinical picture, the course and the familial incidence of the disease, together with the presence of *corps ronds, grains* and *Lücken*, not only a decided resemblance to but also in basic features an evident identity with Darier's disease. On the other hand, any data suggestive of a relation to pemphigus have been conspicuous by their absence, and for this reason even the use of the term pemphigus as a name for this disease has nothing to commend it, except, as Becker stated, "that pemphigus means a bulla."

In the discussion of the cases of Becker and Obermayer, Becker stated that the dominant heredity in this bullous disease is identical with that in cases of Darier's disease. Of the 27 patients with the condition among 78 members of the family in three generations there were 12 males and 15 females, giving about the same sex ratio as among patients with Darier's disease, which is 16 to 18. Becker also stated that the regions involved were characteristic of Darier's disease and that he did not

12. Montgomery, H., in discussion on Becker and Obermayer.[6]

believe the condition could be called pemphigus. But while he, in this manner, made out a strong case for the identity of the two conditions, he expressed the belief that the diagnosis of Darier's disease could be ruled out because: "In the entire family there have been no members with characteristic lesions of Darier's disease, in fact, with papular lesions of any type."

Becker referred to the type of lesion as a vesicular erythematous patch. We can only wonder as to the nature of the "erythematous" base. Ayres and Anderson [3] described lesions in their cases as being papulovesicular. So far as our experience is concerned, the bullae invariably appear on a base composed of coalesced papules. We consider the primary lesion in this disease to be a papule, which may be overlooked because it might be deeply situated or just barely elevated above the skin or because this papular base is obscured by the development of bullae on its surface. Activity of lesions is marked by an almost constant vesiculation or bullous formation, but when involution is about to take place and vesiculation ceases the base comes into view and its papular nature can be observed (fig. 3). In our case we never saw a blister appear on normal skin or on a noninfiltrated smooth macular erythematous base.

A number of dermatoses, such as Paget's disease, certain types of epithelioma, molluscum contagiosum, unusual types of papilloma and verrucae and Bowen's dermatosis, also characteristically reveal their dyskeratotic nature by *corps ronds* and *grains*. However, in these diseases there is not found the feature of multiplication of cells of the basal type, which we consider to be a characteristic phenomenon of the dyskeratosis in Darier's disease and to play a predominant role in the particular form of this disease represented by the bullous process in the cases under discussion. Since this feature is apparently peculiar only to the Darier type of dyskeratosis, it affords an explanation of the presence of the characteristic fissures and lacunas in this disease and their absence in the other dyskeratoses. The consensus as gathered from the literature is that the fissures and lacunas are formed as a result of the separation of the cells by the loss of prickles (*corps ronds*). If the lakelike spaces are produced in this manner, then one would logically expect them to appear in the other dyskeratotic diseases in which *corps ronds* and *grains* are also characteristic elements. But since such is not the case, we are inclined to believe that a distinctive feature of Darier's dyskeratosis is a speeding up or slowing down in the reproductive function of the basal cells (hyperplasia). These cells are incapable of keratinization and are devoid of prickles; so they cannot cohere. As a consequence, the cells remain separated; fluid collects in the potential spaces between them, and the fissures and lacunas are produced.

SUMMARY AND CONCLUSIONS

We originally reported in detail the case of a patient (with a family history of a similar eruption) who presented an unusual and hitherto undescribed bullous dermatosis. The bullae arose on a papular base, and in view of the history, clinical picture, distribution of the lesions, chronic course and, more especially, of a microscopic picture which revealed suprabasal fissuring and *Lücken* together with suggestive *corps ronds* and *grains* and other special features of dyskeratosis, we considered the condition to be a form of Darier's disease with vesiculation.

Subsequently other reports appeared of similar cases. In one report the condition was designated as a form of pemphigus. The majority of observers have proved that the condition is not pemphigus but have regarded it as a process related either to Darier's disease or to epidermolysis bullosa or as a totally independent hereditary and familial bullous dyskeratosis.

In this report we present further studies of our case and a critical survey of the literature, which aim to establish this disease as a bullous form of Darier's disease or at least as a variant of this particular dyskeratosis.

By a comparison of the microscopic observations in our case with those in cases of typical Darier's disease we were enabled to draw at least some tentative conclusions as to the pathogenesis and dyskeratotic phenomena of this dermatosis.

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INOCULATION TUBERCULOSIS

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Primary tuberculous infection of the skin, as contrasted with the reinfection types of external cutaneous tuberculosis, has received considerable attention in recent years. Much earlier knowledge of this type of cutaneous lesion resulted from recognition of the similarity of such infection to the Ghon tubercle in the lung. The pioneer work of Parrot,[1] Kuess,[2] Ghon [3] and others resulted in the establishment, on an anatomic basis, of the character of the lesion produced by first infection tuberculosis. As originally described, the lesion consisted of a primary focus at the site of inoculation plus an always present regional lymphadenitis. To this combination of primary focus and regional lymphadenitis Ranke [4] gave the name "primary complex of tuberculosis," a term rather generally used today when it is desired to designate a primary infection in any part of the body.

GENERAL CONSIDERATIONS

To be sure, the majority of infections of the type under consideration occur in the lung, but those which occur in the skin and the mucosa of the nasopharyngeal, gastrointestinal and genital tracts nevertheless constitute a small but important group. Similarly, cutaneous lesions constitute only a small part of the total number of the primary infections. In a group of 2,000 cases in which all types of cutaneous tuberculosis were represented, Wichmann [5] observed primary infection in 2 per cent. Schürmann [6] reported 4 cases of primary infection, or 0.44

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1. Parrot: Compte rendu des séances de la Société de biologie pendant le mois d'Octobre 1876, Compt. rend. Soc. de biol. **28**:308, 1877.

2. Kuess, cited by Ghon.[3]

3. Ghon, A.: The Primary Lung Focus of Tuberculosis in Children, English edition by D. B. King, New York, Paul B. Hoeber, 1916.

4. Ranke, K. E.: Primäre, sekundäre und tertiäre Tuberkulose des Menschen, München. med. Wchnschr. **1**:305-308 (March 6) 1917.

5. Wichmann, P.: Die primäre exogene Infektion der Haut mit Tuberkulose in ihrer immunisatorischen Bedeutung, Dermat. Ztschr. **53**:717-725, 1928.

6. Schürmann, P.: Der Primärkomplex Rankes unter den anatomischen Erscheinungs- formen der Tuberkulose, Virchows Arch. f. path. Anat. **260**:664-855, 1926.

per cent, in a group of 889 cases of cutaneous tuberculosis. Ghon and Kudlich [7] estimated, on the basis of their material, which included cases of primary infection of all the organs, that only 0.14 per cent of the lesions which they studied were cutaneous lesions. There is still a divergence of opinion regarding some phases of primary tuberculosis, and it is probable that the increasing knowledge and study of the cutaneous complex, since the skin is an accessible medium for study, will serve to clarify some of the controversial data extant on the subject.

External inoculation tuberculosis of the skin includes, in addition to the primary cutaneous complex, the lesions of the reinfection type, such as tuberculosis verrucosa cutis, anatomic tubercles, tuberculosis cutis orificialis and, probably in many instances, lupus vulgaris.

Several excellent reviews are available on the subject of primary cutaneous tuberculosis.[8] Stokes [8d] was the first in this country to call attention to this type of tuberculosis. A year later Bruusgaard [8e] (1926) also reported on the primary cutaneous complex, and since that time the entity has been elevated to an important place in the classification of cutaneous tuberculosis.

Previous to the reports by Stokes and Bruusgaard, Holt [9] (1913) and later Wolff [10] (1921) collected from the literature a group of cases of primary inoculation tuberculosis in which the infection had followed

7. Ghon, A., and Kudlich, H.: Eintrittspforten der Infektion, in Engel, S., and Pirquet, C.: Handbuch der Kindertuberkulose, Leipzig, Georg Thieme, 1930, pp. 20-113.

8. (*a*) Duken, J.: Ueber Verlaufsarten der extrapulmonalen Primärtuberkulose, Ztschr. f. Kinderh. **55**:687-694, 1933. (*b*) Krantz, W.: Der tuberkulöse Primärkomplex an der Haut, Zentralbl. f. Haut- u. Geschlechtskr. **39**:1-19, 1931. (*c*) Michelson, H. E.: The Primary Complex of Tuberculosis of the Skin: Review of the Literature, Arch. Dermat. & Syph. **32**:589-601 (Oct.) 1935. (*d*) Stokes, J. H.: Primary Inoculation Tuberculosis of the Skin with Metastasis to Regional Lymph Nodes, Am. J. M. Sc. **169**:722-736 (May) 1925. (*e*) Bruusgaard, E.: Klinische Beiträge zur Pathogenese der Hauttuberkulose: I. Der primäre Komplex an der Haut; II. Übersicht über die Bedeutung der Stadieneinteilung für unsere Auffassung von der verschiedenen Formen der Hauttuberkulose, Arch. f. Dermat. u. Syph. **152**:465-504, 1926; (*f*) The So-Called "Primary Complex" of Tuberculosis in the Skin, Brit. J. Dermat. **46**:113-126 (March) 1934. (*g*) Goebel, F.: Ueber primäre Hauttuberkulose, Arch. f. Kinderh. **82**:257-262, 1927. (*h*) Kereszturi, C., and Siegel, M.: Primary Tuberculosis of the Skin: Report of Two Cases, Am. J. Dis. Child. **51**:847-855 (April) 1936. (*i*) Laymon, C. W.: Primary Tuberculosis of the Skin, Journal-Lancet **59**:136-138 (April) 1939.

9. Holt, L. E.: Tuberculosis Acquired Through Ritual Circumcision, J. A. M. A. **61**:99-102 (July 12) 1913.

10. Wolff, E.: Ueber Zirkumzisionstuberkulose, Berl. klin. Wchnschr. **58**: 1531-1533 (Dec. 26) 1921.

ritual circumcision. The wounds became infected during the course of the ritual by rabbis who were proved to have had active pulmonary tuberculosis. It has been aptly emphasized, however, by Volk [11] and by Sulzberger and Goodman [12] that these cases—although the conditions are definitely primary infections—should be considered in a group by themselves. Because of the deposition of large numbers of virulent organisms of tuberculosis on the circumcisional wounds, fulminating infections ensued, and approximately 40 per cent of the patients died within the first two years thereafter from generalized miliary tuberculosis. Such a disastrous course is in sharp contrast to that of the usual patient who has a primary cutaneous complex. In the latter event, the disease process usually has a benign course, so far as dissemination of the infection is concerned. No cases of circumcisional tuberculosis have been reported in recent years.

In the most authentic cases of the primary cutaneous complex, the condition has affected children. The reason is obvious because of the relative ease with which previous tuberculous infection can be excluded in children. Negative results of physical examination and negative reactions to the tuberculin test have more significance for the young child than for the adult person. Recent surveys [13] indicate that half to three fourths of the young persons in this country are reaching college age without having had tuberculosis; this would indicate that in the future more primary tuberculous infections of the skin will be encountered among young adults. In the adult person, however, incontestable proof that the infection is primary usually is impossible to adduce.

As pointed out many years ago by Koch,[14] Lewandowsky [15] and Calmette,[16] of all structures of the body, the skin is perhaps the most resistant to tuberculous infection. This probably accounts, in a large measure, for the rarity of the disease under discussion. Some injury to the skin is necessary before inoculation can take place, a fact well

11. Volk, R.: Tuberkulose der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 10, pt. 1, p. 191.

12. Sulzberger, M. B., and Goodman, J.: Tuberculoderms, M. Clin. North America **20**:995-1007 (Nov.) 1936.

13. Hill, L. F., and Kelly, D. H.: Tuberculosis in Children, J. Pediat. **14**: 815-831 (June) 1939.

14. Koch, H.: Die Tuberkulose des Sauglingsalters, Ergebn. d. inn. Med. u. Kinderh. **14**:162-194, 1915.

15. Lewandowsky, cited by Fishberg, M.: Pulmonary Tuberculosis, ed. 4, Philadelphia, Lea & Febiger, 1932, vol. 1, p. 94.

16. Calmette, A.: Tubercle Bacillus Infection and Tuberculosis in Man and Animals, English translation by W. O. Soper and G. H. Smith, Baltimore, Williams & Wilkins Company, 1923.

substantiated by reports in the literature.[17] In most of the reported cases, infection has followed various types of traumatic injury, and inoculation has been reported as occurring in the lesions of impetigo, furuncle, ecthyma and chronic eczema. The site of the majority of the lesions has been the face and the extremities, because these regions are more readily traumatized and more likely to be contaminated by Mycobacterium tuberculosis. There is nothing to indicate, however, that the skin of one part of the body is more resistant than that of another.

NOMENCLATURE

Tuberculous Chancre.—In some of the older textbooks of dermatology the lesions of primary cutaneous tuberculosis were called tuberculous chancre, probably because of the similarity of the lesion to that of primary syphilis. The term is misleading, however, because it tends to focus the attention on the primary lesion rather than on the lesion and the regional lymph nodes. Although it is true that a chancre-like lesion is the most common lesion at the site of inoculation, the primary lesion may be entirely nonspecific in its appearance.

Primary Cutaneous Tuberculosis or Primary Inoculation Tuberculosis.—In recent years most authors have adopted the name primary cutaneous complex of tuberculosis, and, as stated by Krantz,[8b] this is perhaps the best term to use, because it emphasizes both the primary lesion and the always present regional lymphadenitis. However, today physicians and other investigators are familiar with the character of the lesion in primary tuberculosis; so such terms as primary cutaneous tuberculosis and primary inoculation tuberculosis of the skin are acceptable.

Pseudoprimary Cutaneous Complex of Tuberculosis.—Pseudoprimary cutaneous complex of tuberculosis [18] is a term employed for infections which simulate the clinical appearance of the primary complex in patients who have evidence of tuberculosis elsewhere in the body. In other words, the lesions represent a type of reinfection tuberculosis.

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17. (*a*) Chancellor, P. S.: Beiträge zur Frage des Primäraffektes bei der Tuberkulose, Ztschr. f. Kinderh. **10**:12-18, 1914. (*b*) Lutz, W.: Die Hauttuberkulose im Kindesalter, Arch. f. Kinderh. **70**:274-302, 1922. (*c*) Carter, B. N., and Smith, J.: Tuberculous Lymphadenitis Secondary to Inconspicuous Healed Traumatic Cutaneous Tuberculous Lesions, J. A. M. A. **105**:1839-1842 (Dec. 7) 1935. (*d*) Brault, cited by Lutz.[17b] (*e*) Miller, H. E.: Chronic Granuloma in Industrial Dermatology, Arch. Dermat. & Syph. **39**:33-44 (Jan.) 1939.

18. (*a*) Rochat, P.: Etude de superinfections tuberculeuses de la peau (pseudocomplexes primaires) à propos d'une inoculation tuberculeuse de la vulve par contact sexual, Ann. de dermat. et syph. **10**:369-382, 1929. (*b*) Strandberg, J.: A Case of a Pseudo-Primary Tuberculous Complex of the Skin, Acta dermat.-venereol. **18**:611-616, 1937.

Chancriform Tuberculosis.—Chancriform tuberculosis, a term found in French literature, is used to designate tuberculous lesions of the reinfection type and should not be applied to the inoculation tuberculosis under discussion.

ALLERGIC RESPONSE

The type of lesion produced by inoculation tuberculosis of the skin depends mainly on the influence of the immune-allergic state of the person at the time infection occurs, allowing, of course, for other factors, such as the natural resistance of the host and the type, number and virulence of the infecting organisms.

As early as 1891 Robert Koch [19] demonstrated on the skin of guinea pigs the difference between primary infection and reinfection in tuberculosis. He showed that in first infections with Myco. tuberculosis there appeared at the site of inoculation (cutaneous), in about eight to fifteen days, a papule, followed in three to six weeks by the development of lymphangitis and regional lymphadenitis. If guinea pigs were inoculated a second time there was an immediate violent response, often accompanied by necrosis and sloughing at the site of inoculation. Evidence of healing soon appeared. The lesions were localized, and lymphatic metastasis, when it occurred, was much slower in appearing than had been the case in the primary infection; also, the lymph nodes were smaller. He thus established a starting point for the many biologic studies on the immune-allergic phenomena in tuberculosis which have since been conducted. Lewandowsky [20] demonstrated the type of histologic reaction encountered in primary infection as contrasted to that found in reinfection.

SEQUENCE AND SALIENT FEATURES OF PRIMARY INFECTION AND REINFECTION

Primary Infection.—Primary infection in man is similar in many respects to that which occurs in guinea pigs. When an inoculation occurs at a previously uncontaminated site, there is a delayed response or latent period, ranging from one to three weeks, during which the organisms, although multiplying, excite a tissue reaction which is nonspecific in type. It is during this period, probably, that lymphatic extension occurs, although enlargement of lymph nodes is not evident clinically until three to six weeks after inoculation. A negative reaction to the tuberculin test recorded during the first few days of infection proves

19. Koch, R.: Fortsetzung der Mitheilungen über ein Heilmittel gegen Tuberculose, Deutsche med. Wchnschr. **17**:101-102 (Jan. 15) 1891.

20. Lewandowsky, F.: Tuberkulose—Immunität und Tuberkulide, Arch. f. Dermat. u. Syph. **123**:1-75, 1916.

the absence of sensitivity. After a period of six weeks, or a little longer, specific clinical and histologic evidence of tuberculosis is present, and by this time a positive reaction to the tuberculin test indicates the presence of sensitivity. The clinical evidence of specificity marks the change from a primary infection to a reinfection type of lesion, and this is frequently manifested at the site of the primary lesion by a verrucous reaction or lupus nodules. Montgomery and Helmholz [21] have emphasized the diagnostic advantage the physician gains by being able to observe the aforementioned sequence of events in a given instance of primary infection. The appearance of a nonspecific reaction and the occurrence of a negative reaction to the tuberculin test followed later by a specific histologic reaction accompanied by a positive reaction to the tuberculin test make up the classic picture of a primary infection.

Reinfection.—In reinfection of external origin, the infection occurs at a relatively immune and allergic site; the type of lesion varies greatly in clinical appearance, and the condition varies in its course, depending on several factors, such as the degree of allergy and immunity present and the number and virulence of the infecting organisms. In general, however, inoculation in a previously infected person produces a specific reaction within a much shorter interval than that which occurs in a case of primary infection. Lymphatic metastasis seldom occurs in reinfection. It should be mentioned, however, that lymphadenitis has been observed in association with lupus vulgaris, tuberculosis cutis orificialis and tuberculosis verrucosa cutis. In such cases it is probable that the virulence of the infecting organisms was sufficient to overcome the resistance of the host to the extent of allowing lymphatic spread of the infection. A decrease in the immune-allergic state known to occur in some adult persons following the healing of childhood primary complexes probably accounts for the cases of pseudoprimary complex in which the clinical picture and sequence of events may be identical in every respect to those of true primary infection.

BACTERIOLOGIC OBSERVATIONS

The organism which causes bovine tuberculosis has been isolated from the lesions in primary infection in man, but only in rare instances. In this country, in several of the reported cases the condition has occurred among farm children or veterinarians who were probably exposed to the bovine type of infection, but unfortunately the type of organism causing the infection has been recovered only rarely. When the type of organism has been determined, it has been found that Myco. tuberculosis var. hominis is the predominant offender. There is no indi-

21. Montgomery, H., and Helmholz, H. F.: Primary Cutaneous Tuberculous Complex, Proc. Staff Meet., Mayo Clin. **11**:407-410 (June 24) 1936.

cation that the type of lesion produced by the organism of bovine tuberculosis in the primary infection is any different from the lesion caused by Myco. tuberculosis var. hominis. In many of the cases the organisms have been demonstrated in stained smears and histologic sections or by culture and inoculation of guinea pigs with material obtained from the primary lesion or the regional lymph nodes. Tubercle bacilli are much easier to demonstrate in patients seen early in the course of the infection. After the development of the specific tissue reaction, it may be impossible to demonstrate the organisms by any of the aforementioned methods.

HISTOLOGIC CHARACTERISTICS

During the early stage of the disease, the histologic picture of primary cutaneous tuberculosis is nonspecific in type. Ulceration is usually present, and the cutis contains an infiltrate composed of polymorphonuclear and lymphocytic leukocytes and a few plasma cells. Early in the evolution of the lesion the organisms (Myco. tuberculosis var. hominis) are numerous and are usually found in areas of caseation necrosis situated in the infiltrate. After three to six weeks, or about the time that lymphatic extension occurs, more specific pathologic changes may be noted. Epithelioid and giant cells are noted in the upper part and midportion of the cutis as well as in the regional lymph nodes. Later in the course of the infection, the organisms are much less numerous, and it is often impossible to demonstrate them in stained sections. Changes in blood vessels may be present but, if so, are only secondary to the inflammatory process. The histologic picture of primary cutaneous tuberculosis is not typical,[22] in contrast to the pictures of secondary types of inoculation tuberculosis. Decided caseation necrosis is a feature of all types of inoculation tuberculosis of the skin, with the exception of lupus vulgaris. Montgomery [23] has emphasized this feature as a diagnostic point for distinguishing between instances of primary infection in which satellite lupus nodules are evident about the primary lesion and those in which true lupus vulgaris with involvement of the lymph nodes is present.

CLINICAL PICTURE

The most typical picture of primary cutaneous tuberculosis is that seen after involvement of lymph nodes has occurred and before the altered tissue response characteristic of reinfection tuberculosis has made its appearance. The lesion at the site of inoculation usually assumes

22. Dittrich, O.: Zur Klinik und Pathologie der primären Hauttuberkulose, Deutsche med. Wchnschr. **1**:996-997 (June 14) 1929.

23. Montgomery, H.: Histopathology of Various Types of Cutaneous Tuberculosis, Arch. Dermat. & Syph. **35**:698-715 (April) 1937.

the form of a small indolent crater-like ulcer with a rather dry crusted base and a raised, rolled and undermined border, the whole lesion resting on an indurated base which extends into the underlying subcutis. The ulcer simulates strikingly a syphilitic chancre, especially during the first few weeks of involvement of lymph nodes. At times the primary lesion may be represented by a small erythematous nodule which never ulcerates, and in some cases the other extreme is encountered, in which a large scrofulodermatous ulcer is present. It is not uncommon for the lesion to resemble an ordinary nonspecific pyogenic ulcer. Many patients do not present themselves for examination until after a period of several months, at which time the primary lesion may have completely healed. The resulting scar may be surrounded by lupus nodules, or, if the lesion has not completely healed, it may resemble tuberculosis verrucosa cutis or lupus vulgaris.

The involvement of lymph nodes, which occurs during the third week of the infection in most cases, is usually what arouses suspicion of the tuberculous causation of the infection. At first the individual lymph nodes are discrete; but as the infection progresses they become matted together by periadenitis, and after a variable interval liquefaction and rupture occur. The degree of involvement of lymph nodes usually is out of proportion to the degree of reaction in the primary lesion. Lymphangitis with cordlike induration of the channels may or may not be present. At times subcutaneous nodelike swellings are present along the course of the lymphatic vessels, and in some cases, as in infection of the hand, the epitrochlear lymph nodes are involved. Such a condition, however, usually occurs several weeks after metastasis to the axillary lymph nodes has taken place.

DIFFERENTIAL DIAGNOSIS

Usually it is not difficult to prove the tuberculous causation of the lesions under consideration; this is easily determined in most cases by histologic and bacteriologic studies. But to prove that such an infection is primary is usually difficult. The clinical and histologic pictures, although suggestive of primary infection, are not diagnostic. It is necessary to prove without reservation that there has been no previous tuberculous infection. Among young children, in whose cases normal physical conditions and a negative reaction to the tuberculin test have more significance, the diagnosis is made with less difficulty than among adult persons, in whose cases such observations have little if any significance. Even among children allergy varies and may entirely disappear, and the possibility that an infection occurring under these circumstances might simulate a primary complex should be considered. An important aid to the diagnosis of primary infection is the sequence of events, not only in the change from a nonallergic to an allergic reaction, as shown by tuberculin tests, but also in the clinical and histologic sequence, the

delayed specific response at the site of inoculation and an interval of not more than six weeks or two months between infection and lymphatic metastasis.

Palmstierna [24] and Strandberg [18b] have expressed the belief that when swelling of lymph nodes is delayed for more than six weeks or two months, it probably indicates that a certain degree of resistance is present and that the lesion may be interpreted as being indicative of reinfection. This belief is supported by the experimental data of Krause [25] and Willis,[26] who showed that tubercle bacilli inoculated into normal nonallergic guinea pigs could be demonstrated in the lymphatic vessels within twenty-four hours after inoculation. In immune-allergic animals metastasis to lymph nodes occurred at a much slower rate. In man lymphatic extension may occur early in reinfection, and the picture in such an event is identical with that of primary infection.

In most cases the patient is seen only after the infection has been present for some time and also at a time at which the reaction to the tuberculin test usually is positive, so that it is impossible to determine the patient's previous allergic state. By such a time secondary changes usually have occurred in the primary lesion as a result of the altered reaction of the person to infection, so that the lesion may resemble tuberculosis verrucosa cutis or lupus vulgaris. Of course, lupus vulgaris and tuberculosis verrucosa cutis without involvement of lymph nodes and the associated pipe stem lymphangitis are not difficult to distinguish from primary inoculation tuberculosis. At times tuberculosis cutis orificialis may simulate the primary complex, particularly when involvement of lymph nodes is present.

In cases in which a small indolent ulcer with marked induration is presented, distinction of the ulcer from a syphilitic chancre is impossible without microscopic dark field examination and the making of serologic tests and histologic studies. The resemblance of the two lesions is striking during the early course of the tuberculous infection, because at that time the lymph nodes are small and discrete and resemble lymph nodes in the presence of primary syphilis without secondary infection.

Because the lesions of primary cutaneous tuberculosis may be nonspecific in clinical appearance, it may be impossible to distinguish them by clinical inspection alone from ordinary pyogenic ulcer with bubo. In rare instances, epithelioma with metastasis to regional lymph nodes may

24. Palmstierna, K.: Post-Traumatic Primary Tuberculous Infection of the Skin, with a Case History, Acta chir. Scandinav. **70**:249-259, 1933.

25. Krause, A. K.: Remarks on Conditions Necessary to Arouse the Allergic State and on Immunity Through Fixation of Bacteria, Am. Rev. Tuberc. **11**: 343-352 (June) 1925.

26. Willis, H. S.: Studies on Tuberculous Infection: X. The Early Dissemination of Tubercle Bacilli After Intracutaneous Inoculation of Guinea Pigs of First Infection, Am. Rev. Tuberc. **11**:427-449 (July) 1925.

stimulate the primary cutaneous complex, but the two are, of course, easily distinguished by means of histologic examination.

The acute constitutional reaction and positive results of agglutination tests in cases of tularemia will prove the cause of this disease. In subacute tularemia, however, the cutaneous lesion and the regional lymph nodes often present a histologic picture which is similar to that of primary cutaneous tuberculosis. Decided necrosis is found, with an outer zone of epithelioid and giant cells, surrounded by still another zone composed of lymphocytes, which might be confused with the histologic picture of inoculation tuberculosis.

Inoculation tuberculosis, with lymphangitis and lymphadenitis, may in rare instances be confused with sporotrichosis. The multiple nodular lesions along the course of the lymphatic vessels, which are typical of sporotrichosis, are present in some instances of inoculation tuberculosis. A case of this type was reported by Wein and Cornbleet,[27] in which the infection was thought to be sporotrichosis but was later proved to be tuberculosis. In this instance pseudo primary infection probably had occurred, because the patient was shown to have old healed pulmonary tuberculosis.

TREATMENT

In cases of primary cutaneous tuberculosis, a program of treatment directed toward the patient's general health should be instituted. This need not require absolute rest in bed, but ingestion of an adequate diet, including vitamin supplements, should be insisted on. Carefully repeated examinations should be made at frequent intervals to detect any localization of the infection elsewhere in the body.

For the local treatment of the cutaneous lesion and the regional lymph nodes, surgical excision of the primary lesion followed by adequate roentgen ray therapy to the adjacent glands has been used successfully in many cases. In recent years roentgen therapy alone has been used,[28] with satisfactory results. Roentgen therapy is particularly important for lesions on the face, because of the good cosmetic result which can be obtained. Local use of ultraviolet radiation from a quartz mercury vapor glow lamp or from some other source has given good results in the hands of some physicians. The nonspecific or tonic effect of the injection of neoarsphenamine is a valuable adjunct in the therapeutic program. It should be reemphasized that because of the banal appearance of the primary lesions a careful search should always be made for a scar or other local lesion which may be the site of inoculation in any case of superficial tuberculous lymphadenitis.

27. Wein, M. S., and Cornbleet, T.: Inoculation Tuberculosis of the Skin Simulating Sporotrichosis, Arch. Dermat. & Syph. **16**:312-316 (Sept.) 1927.

28. (*a*) Rogin, J. R.: Inoculation Tuberculosis: Scrofuloderma, Arch. Dermat. & Syph. **40**:301 (Aug.) 1939. (*b*) O'Leary, P. A., in discussion on Jamieson, R. L.: Tuberculosis Cutis, ibid. **40**:303 (Aug.) 1939.

PROGNOSIS

Inoculation tuberculosis of the skin, regardless of whether the infection is the primary or the reinfection type, is usually benign, so far as dissemination of the infection to other parts of the body is concerned. Aside from circumcisional tuberculosis, the disease is nearly always confined to the site of the primary lesion and the regional lymph nodes. However, dissemination in rare instances does occur in primary infections. A good example was described by Akerberg:[29] Four years after inoculation in the skin, tuberculous osteomyelitis developed in one olecranon process of the patient; no evidence of tuberculosis in the body could be found which might have accounted for the lesion. Erythema nodosum[30] has been reported to follow primary tuberculous inoculation. The number and virulence of the infecting organisms rather than the natural resistance of the host probably determine whether or not tuberculous foci in other parts of the body will result from infection such as is considered herein. In many of the cases the condition has existed for months before the tuberculous cause has been discovered, and in most of these cases the lesions have remained localized. Local lesions often heal spontaneously. The greatest reaction is present in the regional lymph nodes, and healing is seldom complete at these sites without treatment. In most of the cases in which treatment has been used, adequate local treatment has controlled the infection, and follow-up studies usually show that the infection has remained under control.

Blumenthal,[31] Volk[11] and Dittrich[22] have suggested that the primary complex may be the starting point for lupus vulgaris in some instances because of the frequent occurrence of lupus nodules about the scars of the primary lesions and because of the fact that lupus vulgaris has developed after traumatic injuries. All investigators are not agreed, however, on this point, for according to Schachenmann[32] and Krantz,[8b] the lupus nodules which follow primary infection should be contrasted with those usually found in lupus vulgaris. They pointed out that the lesions which follow primary infection frequently heal with little treatment and that in some instances they may heal spontaneously, which is in decided contrast to lesions in the usual instance of lupus vulgaris.

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29. Akerberg, E.: Zwei Fälle von tuberkulösen Primärkomplexen der Haut bzw. der Gingiva, Acta dermat.-venereol. **14**:127-133 (June) 1933.

30. Rotnes, P. L.: Tuberkulöser Primärkomplex auf der Haut eines Erwachsenen, Dermat. Wchnschr. **95**:1605-1608 (Nov. 5) 1932.

31. Blumenthal, F.: Cutaneous Tuberculosis: Its Relation to the Immune Allergic State, Arch. Dermat. & Syph. **35**:1037-1050 (June) 1937.

32. Schachenmann, G.: Vier Fälle von primärer Hauttuberkulose im Säuglings- und Kleinkindesalter, Sekundäre Lupusbildung, Arch. f. Kinderh. **116**: 33-53, 1939.

REPORT OF CASES

This study entailed a survey of 12 cases of inoculation tuberculosis of the skin observed at the Mayo Clinic. Eight of the patients were males, and 4 were females. Their ages ranged from 2 years to 50.

Clinical and Laboratory Data Obtained from Twelve Cases of Inoculation Tuberculosis *

Case	Age (Years) and Sex	Duration of Infection, Mo.	Antecedent Injury	Primary Lesion (Type and Site)	Time Between Appearance of Lesion and Metastasis to Lymph Nodes	Reaction to Tuberculin Test	Miscellaneous
				True Primary Cutaneous Tuberculosis			
1	4 F	1	Insect bite	Ecthymatous ulcer, left cheek	2 weeks	+†	Acid-fast bacilli demonstrated in sections taken for biopsy
2	8 M	3	Furuncle	Chancriform ulcer, near left eye	3½ weeks	+‡	Guinea pig inoculation positive for tuberculosis
3	2 M	5	Unknown	Scar with satellite lupous nodules following nonspecific ulcer, forehead	Less than 2 months	—	Acid-fast organisms demonstrated in pus from abscess of lymph node
4	5 M	3	Laceration	Ecthymatous ulcer with satellite lupous nodules, left big toe	3 weeks	+	Generalized lymphadenitis; questionable dissemination of infection
5	13 M	4	Laceration	Scar and lupous nodules following nonspecific ulcer, left big toe	3 weeks	+	Guinea pig inoculation positive for tuberculosis
				Diagnosis of Primary Infection Only Presumptive			
6	16 F	2	Furuncle	Chancriform ulcer, right cheek	2 months	—	
7	20 M	6	Laceration	Chancriform ulcer, right cheek	2 weeks	+	Guinea pig inoculations positive for tuberculosis
8	50 M	1½	Abrasion	Chancriform ulcer, right thumb	Axillary nodes, 3 weeks; epitrochlear node, 4 weeks	—	Guinea pig inoculations negative for tuberculosis
9	34 M	12	Unknown	Scar following nonspecific ulcer, left palm	3 to 4 weeks	—	
				Probable Pseudoprimary Cutaneous Tuberculosis			
10	46 M	5	Laceration	Scar with satellite lupous nodules following nonspecific ulcer, left thumb	4 months	+	
11	38 M	12	Unknown	Scar with satellite lupous nodules following nonspecific ulcer, left forearm	10 months	—	
12	31 F	60	Unknown	Scar with lupous nodules following nonspecific ulcer, right cheek	2 years	—	

* In all lesions the histologic picture of inoculation tuberculosis was present. No evidence of previous tuberculous infection was found in the available data of any cases.

† Reaction to tuberculin test was negative at first examination; it became positive in six weeks.

‡ Reaction to tuberculin test was negative at first examination; it became positive in twelve months. Cases 3, 4, 5, 6, 9, 11 and 12 have been reported previously by Stokes (1925).[84]

Efforts were made to demonstrate tuberculous infection, both past and present, by the methods indicated in the table and described in the case reports. Two cases of primary cutaneous tuberculosis and 4 cases of

inoculation tuberculosis in which the diagnosis of primary infection was only presumptive are presented in detail. Three cases of inoculation tuberculosis of the skin with lymphadenitis (pseudoprimary complex) are presented in general terms. Complete data for all 12 cases are given in the table.

CASE 1.—*Primary cutaneous tuberculosis* (case 1 in the table).

A white girl 4 years old was admitted to the Mayo Clinic on Nov. 15, 1934, for treatment of an ulcer of the left cheek. The lesion supposedly had followed an infected bite of an insect one month previously. Two weeks after the onset of the ulcer, a lymph node in the left submaxillary region had become enlarged and tender.

On examination, the child presented what appeared to be an ecthymatous ulcer, 3 cm. in diameter, on the left cheek (fig. 1 *A*) and a rather firm fluctuant submaxillary lymph node on the same side. General physical examination and roentgenograms of the thorax revealed no evidence of tuberculosis elsewhere. A

Fig. 1 (case 1).—Primary cutaneous complex of tuberculosis. *A*, at one month the primary lesion is partially healed and is nonspecific in appearance, and, below, the regional submaxillary lymph node is fluctuant. *B*, the same patient three weeks later shows a beginning verrucous reaction at the site of the primary lesion. The abscess of the submaxillary lymph node has ruptured.

Mantoux test had been done recently, and the reaction to it was found to be negative. There was no evidence of tuberculosis in her family, and her parents knew of no possible contact with tuberculosis elsewhere. The cutaneous lesion was ameliorated slightly by the local application of ammoniated mercury ointment, but the involved lymph node (fig. 1 *B*) gradually enlarged and broke down. Within six weeks from the onset of the infection, the reaction to the tuberculin test became positive, and the cutaneous lesion assumed a verrucous appearance. Histologic examination (fig. 2) of material obtained from a draining sinus over the ruptured lymph node revealed two types of tissue response: (1) a region of necrosis containing many acid-fast bacillary forms, with a peripheral zone of polymorphonuclear leukocytes and a few plasma cells, and (2) an adjacent region of beginning formation of epithelioid tubercles with occasional giant cells but no acid-fast bacilli.

Roentgen ray treatment was administered to both the cutaneous lesion and the draining lymph node. One year after the onset the lesion at the site of inoculation and the lymph node had healed. Two years later the child was examined, but no evidence of activity in the region of either the cutaneous lesion or the lymph node was found. At this time a general physical examination showed no

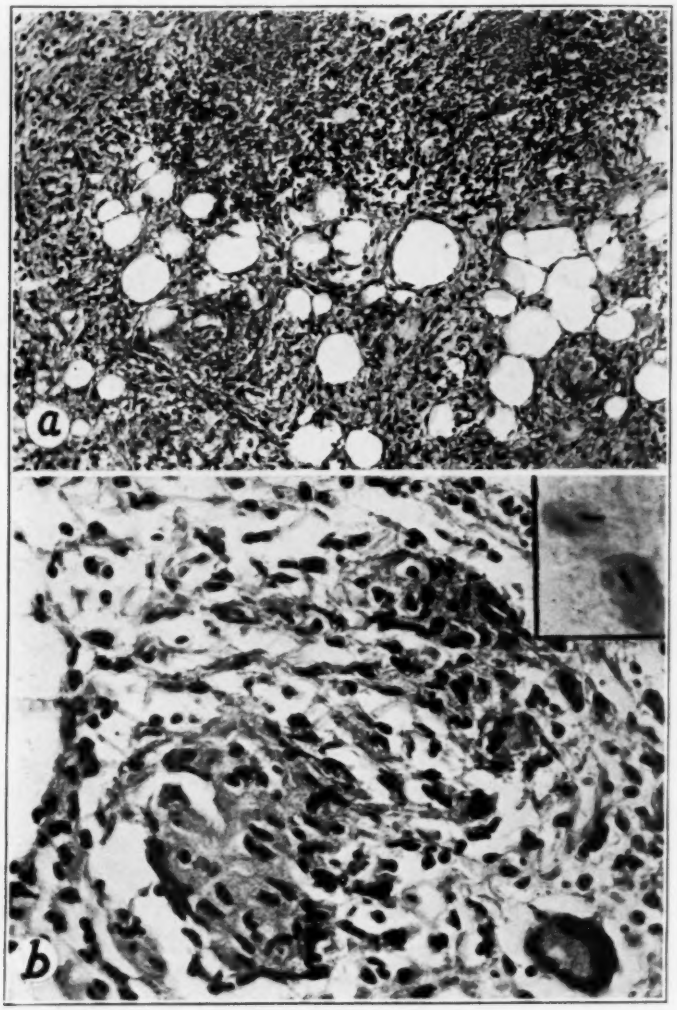

Fig. 2 (case 1).—Histologic sections. *A,* a portion in the oldest part of the lesion, showing an inflammatory infiltrate composed of epithelioid cells, lymphocytes and a few plasma cells; there is a region of caseation necrosis immediately beneath the ulcer, but no specific epithelioid tubercles have formed (hematoxylin and eosin, × 130). *B,* a section of tissue from the periphery of the lesion, in a region of the most recent onset of the disease process, showing early formation of specific epithelioid tubercles and giant cells. There is a beginning specific response (hematoxylin and eosin, × 300). Inset, magnification of the section (*B*), showing acid-fast bacilli in a region near a portion of caseation necrosis (acid-fast stain, × 1,500).

evidence of tuberculosis elsewhere in the body. The reaction to the tuberculin test, repeated at this time, was positive. The patient was examined again in 1939, five years after the onset of infection, and was still in good health at that time.

CASE 2.—*Primary cutaneous tuberculosis.*

A white boy 8 years old was first examined on March 6, 1939. Three months previously his mother had detected an inflammatory papule near the outer canthus of the left eye. Three weeks after the onset of the papule a small ulcer developed, which had remained until the time of the patient's examination.

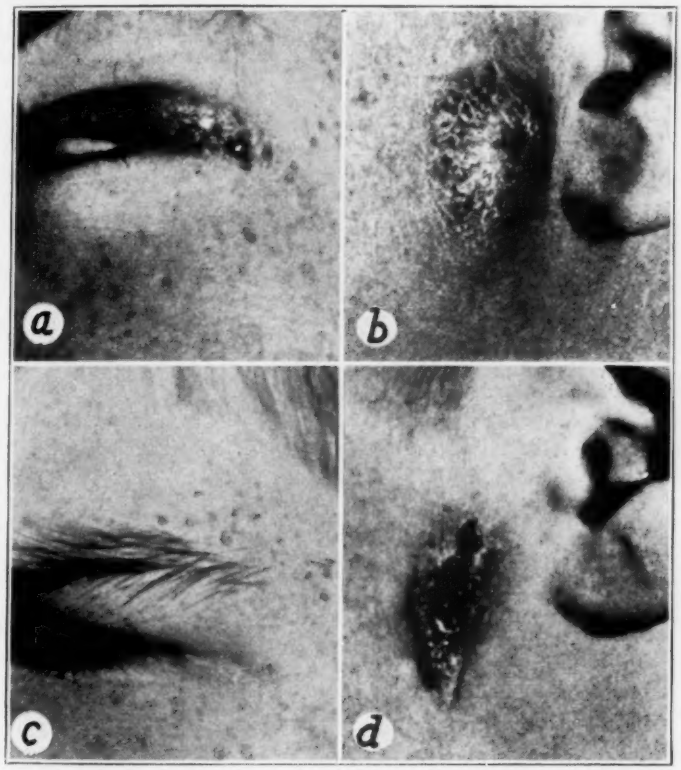

Fig. 3 (case 2).—Primary cutaneous complex of tuberculosis. *A*, chancre-like ulcer near the temporal canthus of the left eye of three months' duration. *B*, fluctuant preauricular lymph node. *C*, primary lesion completely healed after eight months. *D*, nonspecific ulcer at the site of a ruptured abscess of the preauricular lymph node, eight months after onset of the disease.

A few weeks after the appearance of the ulcer, the left preauricular lymph node had become swollen and tender. When the lesion failed to heal, a local physician was consulted. He suspected the tuberculous causation of the lesion and administered a few roentgen ray treatments. There were no associated constitutional symptoms. The history of the patient was not significant except that it included the usual diseases of childhood. No possible contact of the patient with tuberculosis could be determined.

A general physical examination, including roentgenograms of the thorax, showed no evidence of tuberculosis elsewhere in the body. Results of the agglutination test for tularemia were negative. The reaction to a tuberculin test performed at the time of the patient's admission was negative. The test was repeated several times during the course of treatment, and it was not until twelve months after the onset that a positive reaction was obtained. At that time no evidence of tuberculosis elsewhere in the body could be determined which might have accounted for the positive reaction.

Examination of the skin revealed a small crater-like ulcer 2 cm. lateral to the outer canthus of the left eye (fig. 3*A*). The edges of the ulcer were elevated, indurated and slightly undermined. An apple jelly color appeared in the elevated, border of the ulcer when glass pressure was applied, but satellite nodules were not present. The left preauricular lymph node was swollen and fluctuant but not broken down (fig. 3*B*).

Sections from the border of the primary ulcer obtained for biopsy had the histologic aspects of inoculation tuberculosis. Serial sections stained with acid-fast stains revealed no organisms. Examination of smears of material obtained from the primary lesion and from the lymph node also showed no acid-fast bacilli. A portion of the tissue taken for biopsy was pulverized and injected into guinea pigs, but the results were negative for tuberculosis.

During a period of twelve months several roentgen ray treatments were administered to both the primary lesion (fig. 3*C*) and the involved lymph node. At the end of this period the primary lesion had completely healed and the enlarged lymph node had subsided. A nonspecific ulcer which had resulted from the ruptured lymph node (fig. 3*D*) healed after a few weeks. Periodic physical examinations performed during the course of treatment revealed no evidence of dissemination of the infection.

These two patients had typical examples of primary cutaneous tuberculosis. In this group of 5 cases (only 2 of which have been reported) inoculation occurred among children whose ages ranged from 2 years to 13 (table). As previously emphasized, negative reactions to the tuberculin test and the absence of physical evidence of tuberculosis, either past or present, in patients of this age group have more significance than similar observations among older persons. The customary sequence of events in the development of the lesions was present in each case. The interval between inoculation and development of metastasis to the lymph nodes was less than four weeks for the 5 patients in this study who had the primary cutaneous type of infection.

CASE 3.—*Inoculation tuberculosis in which the diagnosis of primary infection was only presumptive* (case 7 in the table).

A man 20 years old was examined on Jan. 9, 1939. Six months previously he had injured the middle knuckle of his right hand during a brawl with a man known to have pulmonary tuberculosis. The patient's knuckle had been lacerated when he struck his opponent in the mouth. The wound showed evidence of inflammation within one week, and during the following three weeks an indolent ulcer developed. Three weeks after injury the left axillary lymph nodes became swollen and tender.

On examination, the usual chancriform ulcer was present at the site of injury, and the axillary lymph nodes were fluctuant (fig. 4). There was no history of previous tuberculosis, and a general physical examination performed on the patient's admission should no evidence of tuberculosis elsewhere in the body. A tuberculin test had not been performed during the first six months of the infection, but the reaction to the test was strongly positive on the patient's admission. A section removed from the edge of the primary ulcer for histologic examination exhibited the typical picture of inoculation tuberculosis (fig. 5). Pus from the axillary lymph nodes which was inoculated into guinea pigs elicited positive reactions for tuberculosis. Both the primary lesion and the involved lymph nodes responded favorably to roentgen ray therapy.

Fig. 4 (case 3).—Patient with inoculation tuberculosis of the skin ("brawl chancre"), probably primary infection, showing a typical chancriform ulcer with an elevated and indurated border on the middle knuckle of the right hand and fluctuant axillary lymph nodes. A section of tissue was removed for biopsy from the edge of the primary lesion.

The ages of the 4 patients who had this type of infection ranged from 16 years to 50. The clinical picture and the sequence in the development of the lesions in each of these patients are compatible with the diagnosis of primary cutaneous tuberculosis, and in all probability some of the patients in this group had primary infections. They are considered in a separate group, however, to emphasize the fact that exclusion of

previous tuberculosis among persons of the ages of the patients in this group frequently is impossible. Old healed primary pulmonary complexes may be impossible to demonstrate, and in many cases the reaction to the tuberculin test may become negative after healing of the lesions. It is true that recent surveys indicate that more instances of primary infection are occurring among adult persons, but this fact is unfortunately of little benefit in the consideration of the individual case.

The Pseudoprimary Complex.—The 3 cases of inoculation tuberculosis of the skin with regional lymphadenitis will be presented in

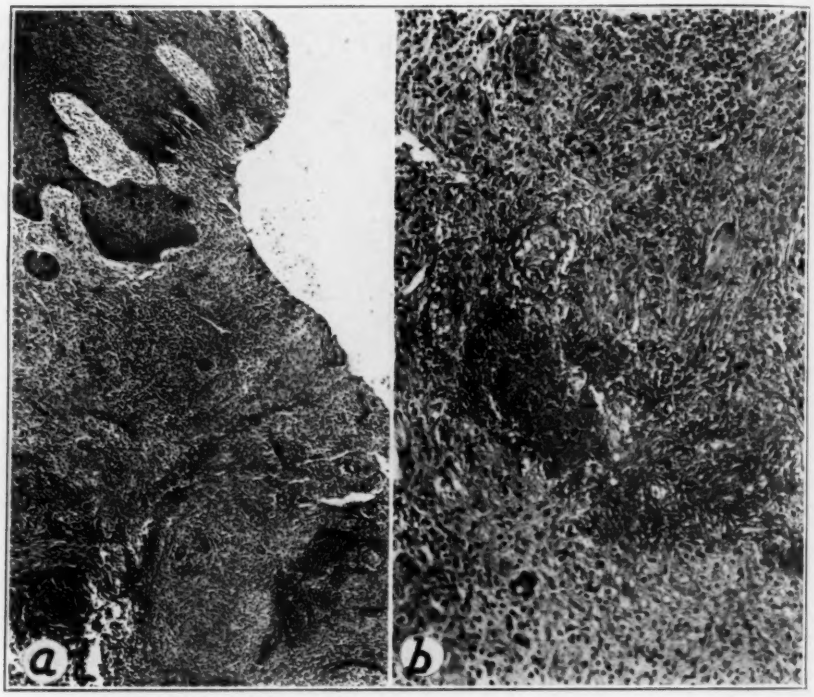

Fig. 5 (case 3).—Histologic section showing: (*a*), an inflammatory infiltrate in the upper portion and midportion of the cutis and a specific epithelioid tubercle in the lower right hand corner of the section (hematoxylin and eosin, × 35); *b*, higher magnification of the same section, showing the epithelioid tubercle and giant cells with caseation necrosis (hematoxylin and eosin, × 145).

general terms (cases 10, 11 and 12 in the table). None of the patients had clinical evidence of tuberculous lesions elsewhere in the body. For these 3 patients, in contrast to those in the preceding cases, the interval between inoculation and metastatic lymphadenitis was four months, ten months and two years, respectively. Aside from this variation, the

lesions at the site of inoculation and the degree of involvement of the lymph nodes simulated those of the primary type of infection. Since it is doubtful that the interval between inoculation and metastatic lymphadenitis ever exceeds six weeks in authentic cases of primary infection, the condition in these cases should be classed as a pseudoprimary complex. Caseation necrosis seen in 1 of these cases (case 11 in the table) is shown in figure 6.

Fig. 6 (case 11 in the table).—Pseudoprimary complex. Section from a regional axillary lymph node, showing a large area of caseation necrosis surrounded by discrete epithelioid tubercles (hematoxylin and eosin, × 50).

COMMENT

Of all 12 cases, a possible source of infection could be determined in only 5. In 1 patient (case 11 in the table), a veterinarian, cutaneous inoculation developed after he had been in contact with tuberculous cows. Unfortunately, the particular type of organism present was not determined in this instance. Most of the patients had been treated for several months by their local physicians, and in only 1 instance was the tuberculous causation of the lesion suspected.

The use of combined surgical and roentgen ray therapy was employed in 3 cases. Eight patients were treated with irradiation alone. The results were satisfactory following both types of treatment. In most cases healing was complete within a few months. Follow-up letters obtained from 8 of the patients from two to twenty years after dismissal revealed that none have had, at the time of this report, recurrence at the site of the inoculation or in the regional lymph nodes.

CONCLUSIONS

A primary cutaneous complex represents the cutaneous analogue of the Ghon tubercle in the lung. Infections usually follow some abrasive injury to the skin which allows the organisms of tuberculosis to gain a foothold.

The cutaneous lesion may be a nodule or a chancre-like ulcer, or it may be nonspecific in appearance. The primary lesion is always accompanied by regional lymphadenopathy with, not infrequently, associated cordlike lymphangitis. The clinical appearance of the lesion is not diagnostic of primary infection. Similar lesions may occur among persons who have previously had tuberculosis (pseudoprimary complex), a fact which makes it difficult to prove that an inoculation of the type that has been described is primary in the case of adult persons.

The sequence in which the lesions develop after inoculation is often helpful in distinguishing between the primary and the reinfection type of cutaneous inoculation tuberculosis.

The most characteristic histologic feature of inoculation tuberculosis is the extensive caseation necrosis. This is present in both the primary and the reinfection type; it is absent in lupus vulgaris.

Primary cutaneous tuberculosis is to be distinguished from tuberculosis verrucosa cutis, lupus vulgaris and tuberculosis cutis orificialis when these lesions are associated with regional lymphadenopathy. Primary cutaneous tuberculosis may simulate ordinary pyogenic ulcer with bubo, syphilitic chancre, epithelioma with metastasis to the lymph nodes, sporotrichosis and subacute tularemia.

The lesions of inoculation tuberculosis are usually benign, so far as dissemination of the infection to other parts of the body is concerned. The lesions usually respond favorably to treatment within a few months.

LYMPHOGRANULOMA VENEREUM

OBSERVATIONS IN ONE HUNDRED AND EIGHTY-SEVEN CASES AT BELLEVUE HOSPITAL

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The recognition of lymphogranuloma venereum as an entity and the new and improved diagnostic procedures have resulted in an apparent increase in the number of cases of this disease. There were 187 patients treated in the dermatologic wards at Bellevue Hospital from 1935 to 1939. Involvement of the inguinal lymphatic glands was twenty times more frequent in men than in women, and there were twice as many patients hospitalized in 1938 as in 1935. The anorectal type of involvement occurred one and one-half times more frequently in women than in men, and the number of patients with this type in 1938 was three times that recorded in 1935. At the Hôpital Saint-Louis in Paris, France, 73 patients were treated from 1931 to 1935.

The classification of the disease into the inguinal and the anorectal type is generally accepted, but, contrary to general belief, lymphogranuloma venereum does not consist of these two types alone. Hellerstrom and Wassén [1] recognized fifty-three primary lesions in 100 cases of the disease; Sézary and Drain,[2] thirty-nine initial lesions in 73 cases. American physicians have been less fortunate in observing patients with the initial lesion. Failure to recognize the primary lesion more frequently may be attributed to several factors. It is usually small, inconspicuous and evanescent. An unsuspected urethritis may be the first manifestation of the disease, which probably follows an initial lesion in the urethra. The incubation period is variable and difficult to determine, owing to the fact that the virus may not become pathogenic for several

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1. Hellerstrom, S., and Wassén, E.: Epidemiology and Etiology of Inguinal Lymphogranuloma, Hygiea **95**:545-586 (Aug. 15) 1933.

2. Sézary, A., and Drain, M.: La fréquence et les formes cliniques du chancre lymphogranulomateux (maladie de Nicolas-Favre), Bull. Soc. franç. de dermat. et syph. **42**:757-760 (May) 1935.

months. Patients do not seek treatment until the appearance of the inguinal lymphatic glandular enlargement. Four weeks after infection is the average time for the appearance of the initial lesion, although conditions occurring as early as five days and as late as several months after contact have been recorded. A so-called nonspecific urethral discharge in which no gonococci can be found should arouse suspicion of a primary lesion of lymphogranuloma venereum located in the urethra. Often the true significance of this type of urethral discharge is not recognized, and a diagnosis of chronic gonorrheal urethritis is recorded.

The initial lesions of lymphogranuloma venereum observed at Bellevue Hospital appeared as a transitory herpetic vesicle, an evanescent erosion, an infiltrated papule, an ulceration and a nonspecific urethritis. In 1 patient the primary lesion was excised, macerated and suspended in saline solution. This material yielded a potent antigen.

It must be emphasized that all patients with genital lesions giving negative reactions for syphilis and chancroid and patients with nonspecific urethritis should be tested for lymphogranuloma venereum by means of the intravenous or intradermal injection of Frei antigen. The incidence and serious debilitating late complications of this disease could be diminished if the diagnoses of ulcer of the penis "cause unknown," nonspecific urethritis and herpes progenitalis were made with the thought that any one of them might be the initial lesion of lymphogranuloma venereum.

THE FREI TEST

Reider and Canizares [3] recently summarized the results of intradermal tests performed at Bellevue Hospital on 116 ward patients suffering from lymphogranuloma venereum and 204 control subjects. The former patients yielded 90 per cent positive, 9 per cent negative and 1 per cent doubtful reactions to mouse brain antigen. The negative reactions occurred in the early stage of the disease, becoming positive later. The control patients gave 93 per cent negative, 5 per cent positive and 2 per cent doubtful reactions to the antigen. The results with mouse brain antigen and with the human antigen were approximately the same, which leads us to believe that they are of equal value in making the diagnosis of lymphogranuloma venereum.

Mouse brain antigen has been used routinely in the dermatologic wards at Bellevue Hospital for more than two years in all patients presenting genital lesions, inguinal buboes and rectal involvement. All of these tests are accompanied by control in the form of an emulsion of

3. Reider, R. F., and Canizares, O.: Evaluation of Frei Test with Mouse Brain Antigen: Comparison with Human Antigen, Arch. Dermat. & Syph. **38**:930-938 (Dec.) 1938.

normal mouse brain. The tests are observed daily and are read on the third and fourth days. The result of the reading depends on comparison of the injection site of the mouse brain antigen with that of the control substance. A decided difference in the amount of infiltration at each site is recorded as a positive reaction if the papule is 7 mm. in diameter or larger. If there is no visible difference in infiltration the reaction is considered negative. The latter type of reaction makes a control test indispensable. It indicates a nonspecific hypersensitivity to foreign protein, mouse brain in this instance, whether or not that protein is free or contaminated with the inactivated virus of lymphogranuloma venereum.

By observing this routine, false positive reactions have been reduced to a minimum, and the intradermal test with mouse brain antigen has

Fig. 1.—Patient with lymphogranuloma venereum. *A*, superficial erosion, a type of primary lesion. *B*, regional lymphadenitis, which was aspirated in an effort to prevent the development of fistulas. *F*, positive reaction to the injection of 0.1 cc. of mouse brain Frei antigen. *C*, site of control test with normal mouse brain.

been found reliable. Negative reactions occur in the early stages of the disease and in cases of negative anergy. One of us (M. J. C.) observed a patient with xanthoma diabeticorum who had a false positive reaction to a Frei test during the time his blood sugar level was high. The reaction became negative while he was under antidiabetic treatment, when his blood sugar level returned to normal. The reaction to an intradermal Frei test with mouse brain antigen usually becomes positive about two to six weeks after appearance of the initial lesion.

Because of the danger of focal and systemic reactions, Frei [4] advised not using the test during the acute stages of the disease. Undoubtedly

4. Frei, W.: On Skin Test for Lymphogranuloma Inguinale: Brief Review and Discussion of Some Possible Causes of Error, J. Invest. Dermat. **1**:367-377 (Oct.) 1938.

such reactions occurred but were attributed to other etiologic factors. They have been rare in our experience.

The intravenous test with Frei antigen, favorably regarded by Hellerstrom and Wassén,[1] was employed by Decker, Canizares and Reider [5] as a check on doubtful reactions to intradermal tests. An elevation of the temperature to 101 F. or higher for a minimum of twelve hours after the intravenous injection of 0.1 cc. of mouse brain Frei antigen is considered a positive reaction. Eighty-five per cent of the patients with positive intradermal reactions also had positive intravenous reactions; the remainder gave doubtful reactions. Of the control subjects, 92 per cent did not react and 8 per cent yielded doubtful results. There were 100 per cent positive reactions to intravenous tests in patients with rectal stricture who also had positive reactions to intradermal

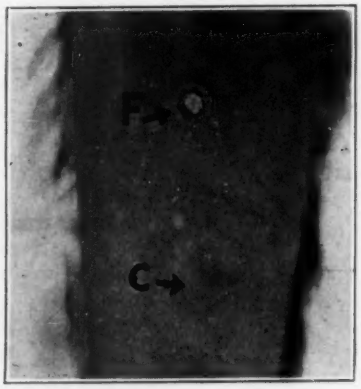

Fig. 2.—Patient with anorectal lymphogranuloma venereum with stricture formation. *F*, reaction with necrosis to the intradermal injection of 0.1 cc. of mouse brain Frei antigen. *C*, reaction to control intradermal injection of normal mouse brain.

tests. The reaction to an intravenous test with Frei antigen is usually positive before that of the intradermal test.

Normal mouse brain injected intravenously caused no elevation of temperature in patients suffering from lymphogranuloma venereum or in controls. There was no sensitization produced by previous cutaneous tests.

Results of the clinical use of the intravenous test confirm the contention of Hellerstrom and Wassén [1] that it is specific. This method of checking doubtful reactions to intradermal tests is accepted as reliable by us.

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5. Decker, D. A.; Canizares, O., and Reider, R. F.: Mouse Brain Antigen, Arch Dermat. & Syph. **40**:397-401 (Sept.) 1939.

The classic clinical picture of chronic inflammatory lymphatic glandular enlargement associated with periadenitis, matting of the nodes and multiple sinus formation with fistulas may be lacking, especially in the early stages, and the differentiation from chancroid is difficult. On the other hand, cases of chancroid resembling lymphogranuloma venereum also occur. In a recent case chancroidal bubo simulated lymphogranuloma venereum so closely that negative reactions to five Frei tests were necessary to convince us that the positive Ducrey reaction was not caused by a previous chancroidal infection.

Mixed infections, caused by syphilis or chancroid, occurred in about 3 per cent of our cases. Because of the permanency of a positive reaction to a test with Frei antigen in old cases of lymphogranuloma venereum, a reliable history is necessary, in addition to the clinical and laboratory findings, for accurate diagnosis of the infection.

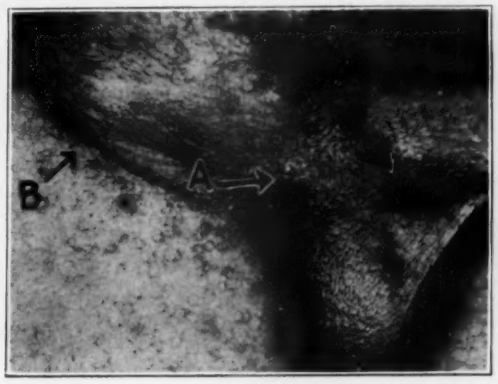

Fig. 3.—Patient with lymphogranuloma venereum. *A*, herpetic vesicle, initial lesion. *B*, regional lymphatic glandular enlargement before the development of multiple fistulas.

Extragenital lesions involving the mouth have been reported.[6] A patient with simultaneous involvement of the inguinal and cervical lymphatic glands was reported by us recently.[7] The diagnosis was confirmed by the preparation of a potent antigen from the aspirated material from the affected lymphatic lymph glands, both inguinal and cervical. Positive reactions to intradermal tests with this antigen were

6. Curth, W.: Extragenital Infection with Virus of Lymphogranuloma Inguinale, Arch. Dermat. & Syph. **28**:376-380 (Sept.) 1933. Bloom, D.: Lymphogranuloma Inguinale of the Tongue and Cervical Glands, ibid. **28**:810-819 (Dec.) 1933.

7. Costello, M. J., and Cohen, J. A.: Lymphogranuloma Venereum Affecting Simultaneously Cervical and Inguinal Lymphatic Glands, Arch. Dermat. & Syph. **41**:557-561 (March) 1940.

obtained in cases of proved lymphogranuloma venereum and negative reactions to intracutaneous tests in control patients free of the disease (inverted Frei test).

TREATMENT

The introduction of sulfanilamide was followed by encouraging reports concerning its efficacy in lymphograuloma venereum. Shropshear [8] reported clinical and subjective improvement in cases of rectal involvement following the administration of 30 grains (2 Gm.) of sulfanilamide daily for two week periods separated by seven to ten day rest intervals. The number of treatment periods varied with the individual response. We have treated effectively over 25 patients in the dermatologic service at Bellevue Hospital suffering from lymphogranuloma venereum with large initial doses of sulfanilamide, 80 grains (5.2 Gm.) a day for the first three days, and 30 grains daily for relatively long periods, with practically no toxic manifestations of the drug. This therapy is especially indicated in the early stages of the disease before massive suppuration and sinus formation develop. It is also efficacious in curing the early proctitis associated with this infection. The prompt administration of sulfanilamide is imperative in the early stages to help prevent the distressing late sequelae, such as anorectal stricture and esthiomene. We believe that the combination of sulfanilamide therapy with intravenous injection of Frei antigen offers the best treatment of lymphogranuloma venereum at present. This is especially true in ameliorating the symptoms and signs of anorectal involvement in the later stages of the disease. Proctoscopic examinations confirm the clinical improvement. Sulfathiazole has been used recently and has given equally good results.

Knight and David [9] reported dramatic response to sulfanilamide in several hopeless cases of anorectal stricture. Our experience with sulfanilamide in the anorectal type of the disease has been that it is of value only in controlling infection with secondary pyogenic organisms.

It has also been administered in rectal suppositories, with good results.

Treatment with sulfanilamide orally and with Frei antigen intravenously, either alone or combined, has proved to be most effective.

In addition to the aforementioned therapy typhoid vaccine, antimony and potassium tartrate U. S. P., fuadin and cholesterolized bismuth have been used in the dermatologic service at Bellevue Hospital. The many and varied treatments prove that no single method of therapy is out-

8. Shropshear, G.: Sulfanilamide in Treatment of Strictures of Rectum Caused by Lymphogranuloma Venereum, Illinois M. J. **74**:153-156 (Aug.) 1938.

9. Knight, A. A., and David, V. C.: Treatment of Venereal Lymphogranuloma with Sulfanilamide, J. A. M. A. **112**:527-529 (Feb. 11) 1939.

standing save sulfanilamide. Favorable response to bed rest and to aspiration of the unruptured buboes occurs frequently. How effective this combined method of therapy will be in a large series of cases remains to be seen.

CONCLUSIONS

1. The primary lesion of lymphogranuloma venereum, occurring in the form of a herpetic vesicle, as an evanescent superficial papule or ulceration or as a nonspecific urethritis, is seen more frequently than is generally thought. The initial appearance of lymphogranuloma venereum as a nonspecific urethritis should be emphasized.

2. Mouse brain antigen is as reliable as human antigen in the performance of the intradermal Frei test. A control test with normal mouse brain is essential.

3. The intravenous test is a specific check on the intradermal test, and the reaction may be obtained before that of the intradermal test can be demonstrated.

4. Sulfanilamide by mouth and Frei antigen intravenously or a combination of the two appears to be the most efficacious means of controlling this disease and of helping to prevent the debilitating anorectal involvement. Further studies of the therapeutic effects of these agents, administered separately and combined, are indicated.

5. Early routine proctoscopic examinations should be performed on all patients suffering from lymphogranuloma venereum, as our observations have led us to believe that proctitis, the forerunner of the anorectal stricture, may be an early manifestation of the disease in both sexes.

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KERATOSIS BLENNORRHAGICA

REPORT OF TWO CASES

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Keratosis blennorrhagica was first described as a clinical entity by Vidal,[1] in 1893. Simpson [2] was the first in the United States to describe a case. The paper published by Keim [3] in 1924 is a classic contribution to the histopathology. The analysis by Epstein [4] in 1939 is an excellent summary of the disease and clarifies the differences between keratosis blennorrhagica and psoriatic arthropathica. As shown in this last article, there have now been over 100 cases reported, yet only 75 were sufficiently well described to be used in the study. Two cases are here reported: one, merely to add another complete study to the literature of this rare disease, and a second, to present an interesting possibility in differential diagnosis.

REPORT OF CASES

CASE 1.—L. C., a 32 year old white man, entered the medical service of the University of Virginia Hospital on Dec. 18, 1939, with the complaint of sore joints. The tentative diagnosis was atrophic arthritis. Because of the peculiar keratoses on the soles, the patient was transferred to the dermatologic service.

History.—The patient had felt well until ten weeks prior to admission, when soreness in the right hip developed. After remaining localized for five days the soreness involved other joints at intervals of several days. During the two weeks prior to admission the pain subsided in all joints except the right knee, which ached constantly. Moderate swelling was present without noticeable redness. Ten days after the onset of joint involvement the patient noticed knoblike elevations on his palms and soles. In addition, the plantar surfaces of the feet were greatly thickened, giving the patient the sensation that he was "walking on a solid block." At this time the patient noticed round plaques of yellowish waxy material on his

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1. Vidal, E.: Eruption généralisée et symétrique de croûtes cornées avec chute des ongles, d'origine blennorrhagique, coincident avec une polyarthrite de même nature. Récidive à la suite d'une nouvelle blennorrhagie deux ans après la guérison de la première maladie, Ann. de dermat. et syph. **4**:3, 1893.

2. Simpson, F. E.: Kératodermie Blennorrhagique, with Report of a Case, J. A. M. A. **59**:609 (Aug. 24) 1912.

3. Keim, H. L.: The Histogenesis of Keratoderma Blennorrhagicum, Arch. Dermat. & Syph. **9**:423 (April) 1924.

4. Epstein, E.: Differential Diagnosis of Keratosis Blennorrhagica and Psoriasis Arthropathica, Arch. Dermat. & Syph. **40**:547 (Oct.) 1939.

scalp. The lesions on the scalp and feet had persisted; the palmar lesions, however, had subsided, leaving only slight residual hyperpigmentation.

Further questioning revealed that the patient first contracted gonorrhea at the age of 17. All symptoms subsided after six weeks of active treatment. At the age of 21 the patient was confined to bed for three months with arthritis, similar to the present illness. Recovery was spontaneous; no keratoses were observed. At the age of 27 the patient contracted a second gonorrheal infection and was again symptomatically relieved after five weeks of treatment. After that the patient was free of nocturia, dysuria and frequency.

He stated that he had no previous eruption other than the dermatologic manifestations of the childhood exanthemas. Despite a good appetite, the patient recently

Fig. 1 (case 1).—*A*, keratosis with numerous knoblike growths. Scaling can be observed. *B*, "dirty beeswax" cast of the little toe with the toe nail included.

lost 40 pounds (18 Kg.) in weight. There was no family history of any scaly eruption.

Physical Examination.—The temperature, pulse and respirations were normal. The patient was well developed but appeared poorly nourished. He was cooperative but nervous and apprehensive. On the entire surface of the soles was a decided keratosis, particularly on the pressure parts. In addition, there were observed on each foot eight to ten guttate, dome-shaped waxy horny knobs, 6 to 8 mm. in diameter. On removal of a thick flat layer of keratotic skin, a horny knob would occasionally be found underneath. Ordinarily, however, when the keratosis was peeled off the exposed skin appeared slightly erythematous and the edges were rough and scaling. The keratosis involved the pads, sides and ends of the toes in the formation of irregular knobs resembling dirty beeswax molds (fig. 1). The keratotic changes under the free edge of the nails were slight but

sufficient to cause some separation of the nail from the nail bed. On the crown of the scalp there were four round seborrhea-like plaques, 1.5 to 3 cm. in diameter, several millimeters thick in the center and thinning at the periphery. They were pierced by the hair shafts. The scales were easily removed, leaving apparently normal scalp. On the glans penis and on the distal portion of the prepuce, mainly around the corona, were noted erythematous areas of smooth "new" skin, some of which had thin keratotic plaques, thickest in the center and tapering off at the edges. In the thenar and hypothenar areas of the hands there was slight increase in pigmentation, corresponding to the areas where the patient recently had had an involvement similar to that on the feet. The right knee, the fourth toe on the left foot, the right metatarsal region and the right sternoclavicular joint appeared moderately swollen. All were slightly tender; however, motion was not restricted. Considerable muscular atrophy was present in both legs and about the right shoulder. The prostate was enlarged, firm and easily outlined.

Observations and Laboratory Data.—At the time of the patient's admission the red blood cell count was 3,800,000; the hemoglobin amounted to 12 Gm. per hundred cubic centimeters, and the white cell count was 9,600, with a normal hemogram. The urine was normal except for the presence of 10 to 30 pus cells per microscopic field. The Wassermann and Kahn reactions of the blood were negative. The sedimentation rate was increased, with a fall of 20 mm. in ten minutes, 30 mm. in twenty minutes and 32.5 mm. in one hour. Blood cultures showed no micro-organisms. There were 1.8 mg. of uric acid and 160 mg. of cholesterol per hundred cubic centimeters of blood. The basal metabolic rate was ±0 per cent. Sodium hydroxide preparations of the skin scrapings showed no fungi, and no growth was obtained on Sabouraud's medium. Cultures of scrapings from the keratoses revealed anaerobic and aerobic nonhemolytic Staphylococcus albus and Bacillus subtilis, with occasional Streptococcus hemolyticus and Staphylococcus aureus. No evidence of gonococci could be found by repeated cultures of smears. A complement fixation test for gonorrheal infection gave a negative reaction with the blood but a strongly positive reaction with fluid obtained by aspiration of the right knee joint. The Wassermann reaction of the same fluid was negative. A roentgenogram of the right knee showed only slight thickening of the joint capsule, considered to be synovitis.

Although there were no urologic complaints at the time, the history of repeated attacks of gonorrhea associated with a slightly enlarged boggy prostate with pyuria established a diagnosis of chronic gonorrheal prostatitis. A three glass test showed 20 pus cells per microscopic field in the first and second glasses and 30 to 40 cells in the third glass. A Gram stain of the specimen in the third glass revealed gram-negative intracellular cocci and rods in small groups and clusters.

Course in the Hospital.—While in the medical service the patient had been given large doses of acetylsalicylic acid, without apparent results. After the diagnosis of chronic prostatitis had been made, the patient received 40 grains (2.6 Gm.) of sulfanilamide daily and prostatic massage at four day intervals. A high vitamin, high caloric diet was given. Under this routine the patient's arthritis gradually subsided to mere stiffness of the joints. The seborrheic plaques observed in his scalp gradually became detached after a week, and no new lesions developed. The penile eruption had a macerated surface, which gradually became less hyperkeratotic until it was only a thin layer of softened tissue. Without local treatment the lesions on the soles remained essentially unchanged for several weeks, and then gradually the keratosis became loosened and could be easily

removed mechanically. The skin beneath was usually smooth, soft and erythematous, but in some areas a slight residue of the keratotic layer produced a pale irregular velvety appearance. The keratosis of the right little toe was observed to be loose; slight force painlessly removed in one piece a cast of the top and sides of the entire toe, with the toe nail included (fig. 1*B*).

When the patient was discharged on Jan. 19, 1940, his only complaint was weakness. The right sternoclavicular joint, the right foot and the left fourth toe were still somewhat swollen but not tender. No crusting remained. The patient's prostate at this time was normal in consistency. Only 4 to 5 pus cells per microscopic field could be found in the urine after prostatic massage.

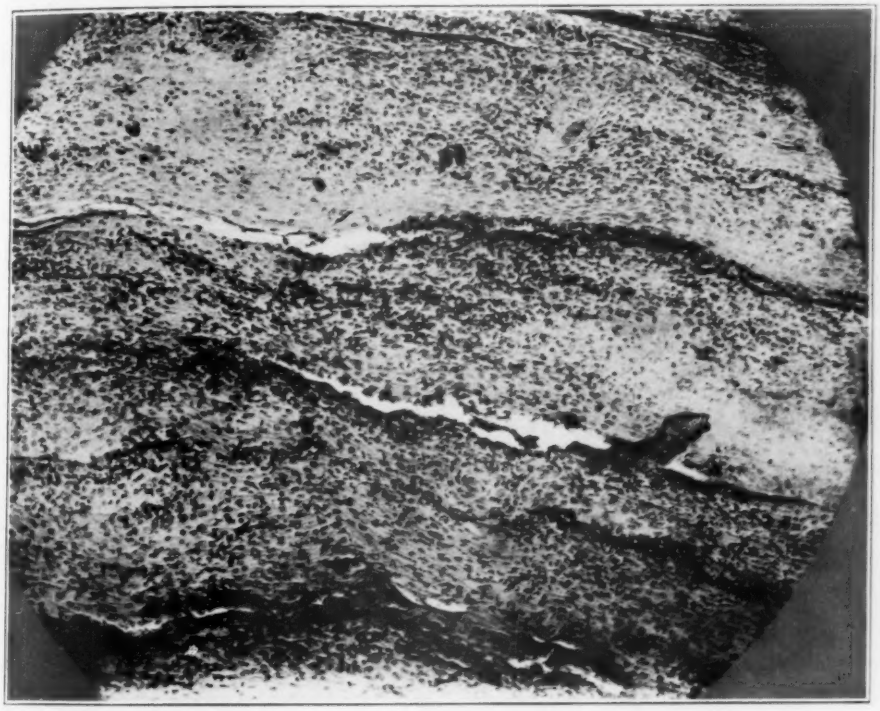

Fig. 2 (case 1).—Crust showing parakeratosis with lamellated cellular infiltration.

Follow-Up Study.—On March 11, 1940 the patient returned to the hospital for observation. He stated that he felt well and had gained 28 pounds (12.7 Kg.) in weight. He complained of slight swelling and a feeling of weakness in his knees and of occasional sharp jabs of pain in the arch of the right foot. The areas which had been involved with keratoses were entirely normal except for a slight erythema. Moderate seborrheic dermatitis of the scalp and ears was present. Rectal examination revealed a prostate of normal size and consistency. A complement fixation test of the blood for gonorrheal infection again gave a negative reaction. The three glass urine test after prostatic massage revealed 0 to 2 pus cells per microscopic field.

Histologic Studies.—Three biopsy specimens were taken. The first, on Dec. 20, 1939, consisted of a section of a knobby crusted lesion from the left foot. Micro-

scopically there was a heavy crust, consisting of parakeratosis embodied in which were lamellated collections of degenerated nuclei of small round cells. The stratum granulosum was entirely absent; however, in that region there were several layers of loosely attached parakeratotic cells, in which a considerable infiltration with polymorphonuclear neutrophils and small lymphocytes was noted, particularly in the suprapapillary areas. The malpighian layer itself had considerable acanthosis with elongation and a somewhat irregular broadening of the rete cones; intracellular and intercellular edema was present. The infiltration throughout this layer with lymphocytes and polymorphonuclear neutrophils was slight, except for that noticed in the suprapapillary area. The papillae were edematous and were infil-

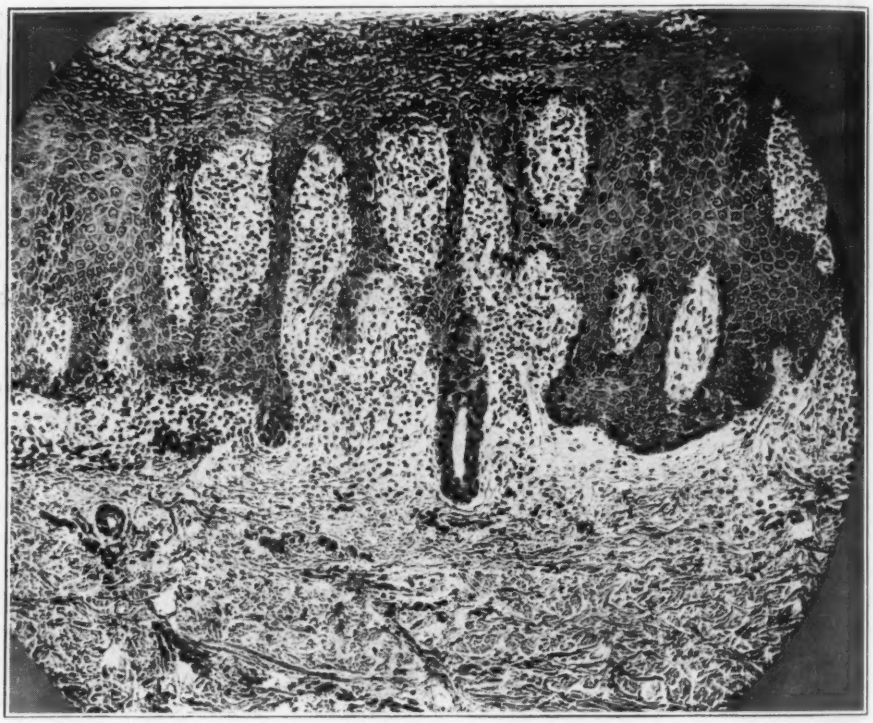

Fig. 3 (case 1).—Corium showing acanthosis, spongiosis, edema of the papillae and cellular infiltration.

trated with small round cells, including a few plasma cells. The blood vessels of the papillary and subpapillary layers were dilated. The endothelial cells were thickened, and considerable perivascular infiltration, mainly with lymphocytes, was noted. MacCallum and Goodpasture stains failed to reveal any gram-negative organisms.

The second histologic specimen, taken on Dec. 30, 1939, was from a lesion on the right heel. The site of election was considered to be an area showing the most activity, although it appeared somewhat older than the section removed for the first histologic examination. The crust in this instance presented no parakeratosis. Some of the degenerative nuclei of small round cells were present in the hyperkeratotic crust. The stratum granulosum was prominent. The malpighian

layer showed acanthosis, though not to as great a degree as was seen in the previous specimen. Only slight perivascular infiltration was present in the corium; however, there could still be found a slight lymphocytic invasion of the malpighian layer.

The third section, taken on Jan. 8, 1940 from the left sole, revealed a loosely lamellated thick hyperkeratotic crust, again with no parakeratosis. The stratum granulosum was thickened in some instances to four layers. The rete cells presented slight intracellular edema. Practically no round cell infiltration was noticed. Decided acanthosis, however, still persisted. The rete cones were broad and not finger-like in structure. The papillae were only slightly edematous, but a moderate

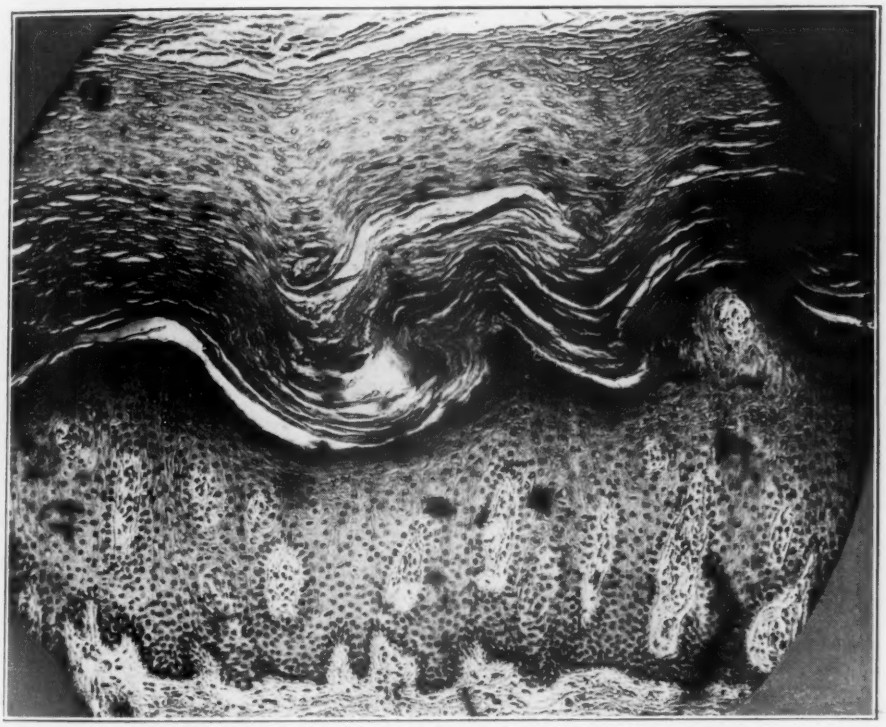

Fig. 4 (case 1).—Epidermis from lesion similar to that in figure 2 though showing no parakeratosis.

small round cell infiltration was present, particularly about the vessels in both the papillary and the subpapillary layer.

CASE 2.—E. P., a 29 year old white married man, was first seen by us in consultation on Dec. 22, 1939, when he complained of several "sores" on his penis of two weeks' duration. The patient was in the orthopedic service of the University of Virginia Hospital with a diagnosis of chronic infectious arthritis of both knees, chronic prostatitis and anal fissure.

History.—He had his first attack of gonorrhea in 1931. The second followed in December 1935. Several weeks later severe pain developed in both knees, and on Jan. 13, 1936 he was hospitalized in a marine hospital, where diagnoses of acute gonorrheal urethritis and gonorrheal arthritis were made. During this four

and one-half month hospitalization there first developed sores similar to those now present, except that they were not as large, and they cleared up after several weeks without treatment.

When he was readmitted to that hospital in September 1936 he had a recurrence of the penile lesions. On this occasion a diagnosis of chronic gonorrheal infection of the prostate gland was added. Despite treatment, the patient's arthritis continued to become worse, and in June 1939 during an accentuation of symptoms he was seen at the Johns Hopkins Hospital, Baltimore. There, in the genitourinary dispensary, a diagnosis of chronic prostatitis was made, and in addition it was noted that the penis was "covered with numerous maculopapular lesions on the corona and the glans."

Fig. 5 (case 2).—Penile lesion showing sharp outline with irregular raised surface and crust formation.

The patient was first seen in the University of Virginia Hospital in October 1939, when a synovectomy was performed on the right knee. Postoperative recovery and the final result were good. However, on November 25, two days after sexual intercourse, the patient again had a urethral discharge, accompanied by considerable swelling of the left knee and the appearance of several excoriated areas on the penis. The arthritis became progressively worse, involving the knee recently operated on, and the patient was again hospitalized on December 21. The past and family history were negative for scaly eruptions.

Physical Examination.—The temperature, pulse and respirations were normal. The patient was moderately well nourished. He was in some pain, owing to the involvement of the joints, inspection of which showed swelling and tenderness, particularly in the knees but also in the ankles. Flexion of the right knee was

limited to 35 degrees; of the left knee, to 110 degrees. On the glans penis, corona and adjacent foreskin were four erythematous, annular, marginated, superficial, flat, dry lesions. They were 1 to 3 cm. in diameter and appeared erosive. No ulceration was present. The prostate gland was moderately enlarged and rather boggy.

Laboratory Findings and Observation.—The results of routine urinalyses were always essentially normal except for the presence of pus cells, 0 to 10 per microscopic field. The red blood cell count was 3,750,000; the white blood cell count was 7,800, with 64 per cent polymorphonuclear neutrophils. The Wassermann and Kahn reactions of the blood were negative. Despite the fact that the patient had received a course of gonococcus vaccine while in the marine hospital in 1936,

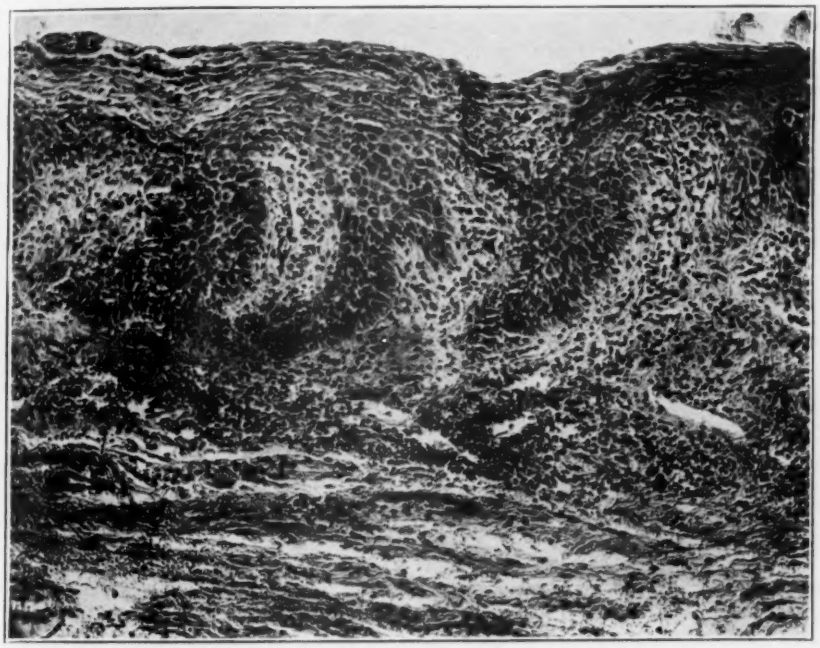

Fig. 6 (case 2).—Spongiosis and degenerative effects in rete, which might be confused with early dyskeratotic changes.

the result of a complement fixation test of the blood for gonorrheal infection was negative. The sedimentation rate was considerably increased, with a drop of 27 mm. in thirty minutes and 30 mm. in sixty minutes. A roentgenogram of the right hip was consistent with a diagnosis of infectious arthritis; the joint was almost obliterated.

Course in the Hospital.—During his stay the patient received seven fever treatments by means of intravenous injection of typhoid bacilli. Prostatic massage was given repeatedly. Sulfanilamide was given for a week. The orthopedic condition improved slowly and slightly. The penile lesions persisted as first observed for several weeks and then became covered with a thin, flaking type of crust, which was superimposed on a sharply defined, slightly elevated, indurated, erythematous base, closely simulating a psoriatic lesion. Several of the areas

increased in size, whereas one was observed to clear up completely. At no time were there any subjective symptoms. Potassium permanganate soaks and local applications of tincture of merthiolate 1:1,000 were used, apparently without exerting any influence on the course of the disease.

Histologic Study.—The only specimen for histologic study was taken on Feb. 1, 1940 from a lesion on the foreskin which had passed into the scaling stage. The stratum corneum was thickened and consisted mainly of parakeratotic cells. The layer had a somewhat patchy, moderately heavy infiltration with small round cells in various stages of degeneration. The stratum granulosum was absent; the rete was acanthotic, with elongated, broad cones. Intracellular and intercellular edema and small round cell infiltration with polymorphonuclear neutrophils and small lymphocytes were present. The papillae were edematous and infiltrated with polymorphonuclear neutrophils, small lymphocytes and occasional plasma cells. The subpapillary layer was hyperemic and heavily infiltrated, mainly with small lymphocytes. The endothelial cells were prominent.

Follow-Up Study.—When the patient returned to the hospital on April 29, 1940, eleven weeks after discharge, he stated that the lesions on the skin had cleared about March 1, 1940, having persisted for three months. During a recent period of hospitalization (March 1941) it was learned that throughout the past year the patient had had severe arthritis. He had had several penile lesions during that time and had observed that he could precipitate an eruption by allowing the foreskin to remain over the glans.

COMMENT

The condition in the first case was a typical example of keratosis blennorrhagica. The diagnosis could be easily made, and aside from the ruling out of unrelated conditions, such as hyperkeratosis of the soles due to fungi and arsenical keratoses, the only disease presenting a real differential problem was psoriasis with arthritis. The freedom of involvement of the areas usually affected by psoriasis, the nature of the lesions themselves and a history of loss of weight, repeated attacks of gonorrhea, an associated arthritis and no previous eruption readily suggested the correct diagnosis, which was confirmed by histologic study. The first section (figs. 2 and 3) showed a picture of the disease, simulating the end stage or stage of crusting described by Keim [3] and the "parakeratotic rupial lesion," or final stage, described by Lees and Percival.[5] The second and third sections (fig. 4), though grossly essentially the same as the first, microscopically presented only hyperkeratosis. Thus it is possible for typical clinical keratosis blennorrhagica to show no parakeratosis histologically. By corollary, lesions of this disease evidently subside by loss of the parakeratosis while still maintaining a hyperkeratosis.

The condition in the second case represents the so-called abortive or balanitiform blennorrhagic keratosis. Again the diagnosis was easily

5. Lees, D., and Percival, G. H.: Keratoderma Blennorrhagicum: Its Histology, Clinical Characteristics and Treatment, with Report of Eight Cases, Lancet **2**:1116 (Nov. 21) 1931.

established when the entire history with interrelation of the keratoses to the urethritis and arthritis was recognized. However, to complicate this case, the patient did not state that he had had previous penile eruptions, and thus an interesting problem in differential diagnosis was presented. Herpes progenitalis was easily excluded by the nonsensitive broad papular nature of the lesion. Syphilis was not considered seriously enough to even warrant dark field studies, although repeated serologic examinations were made. Psoriasis was considered unlikely because no other lesions of the skin were present and because there had apparently been no other attack; histologic examination ruled it out.

Although no particular consideration has been previously made of the differential diagnosis of keratosis blennorrhagica and erythroplasia of Queyrat, it was of prime importance in this case. The lesions consisted of erythematopapular patches, simulating most descriptions of that erythroplasia. Unfortunately, no picture was taken of the second patient's lesions before the crusting appeared; however, the full color illustration of psoriasiform carcinoma of the penis in the March 1940 issue of the *British Journal of Dermatology and Syphilis*[6] could have passed for an exact reproduction of this patient's lesions. When this patient was first photographed, on the lesions had developed a thin, dry crusted surface, a change not infrequently seen in early malignant conditions. There were many histologic features which made the condition consistent with erythroplasia of Queyrat. Frankly, the condition was thought for some time to represent that precancerous dermatosis, and in view of the present plan of early radical treatment of such lesions, severe consequence might have resulted had not the case been investigated further. The true nature of the disease was demonstrated by its healing, leaving only slight erythema to indicate the involved areas. The discovery of the numerous previous episodes, of course, established the diagnosis.

From casual observation, the 2 cases here presented are decidedly different; however, close analysis shows many points of similarity. Each patient was a man who had had repeated attacks of gonorrheal urethritis with associated severe arthritis, for each the cause of hospitalization. Each had demonstrable changes in the genitourinary tract. One had multiple areas of cutaneous involvement; the lesions of the other were limited to the penis, yet histologic examination showed essentially the same process; maceration due to location accounted for some apparent inconsistencies. One patient was obviously bothered and somewhat incapacitated by the cutaneous lesions, while the second patient had no inconvenience from the eruption.

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6. Savatard, L.: Psoriasiform Carcinoma of the Penis, Brit. J. Dermat. **52**:87 (March) 1940.

SUMMARY AND CONCLUSIONS

Two cases of keratosis blennorrhagica are presented; in 1 the condition was generalized and in the other localized.

In the subsiding stages of the disease, all the factors necessary for a diagnosis may be present, yet the histologic sections may show no parakeratosis.

Erythroplasia of Queyrat should have an important place in the differential diagnosis of this disease.

GIANT FOLLICULAR LYMPHADENOPATHY

ASSOCIATION OF GIANT FOLLICULAR LYMPHADENOPATHY AND ITS POLYMORPHOUS CELL SARCOMA DERIVATIVE, SYMMERS' DISEASE, WITH LESIONS OF THE SKIN

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In recent years there have appeared in medical literature reports of a new pathologic and clinical entity under various titles, among which are giant follicular lymphadenopathy, follicular lymphoblastoma and giant lymph follicle hyperplasia of the lymph nodes and spleen. The interest of dermatologists has recently been aroused by the observation of Symmers [1] that there are certain persons in whom there is a relation between universal chronic erythroderma and local or generalized enlargement of the superficial lymph nodes with the histologic characteristics of giant follicular lymphadenopathy and/or its immediate derivative, the polymorphous cell sarcoma of the lymphoid follicles.

In the last two years we have observed 15 patients whose excised superficial lymph nodes have showed the aforementioned histologic changes. Clinical diagnoses included contact dermatitis, exfoliative dermatitis (Wilson and Brocq), psoriasis, dermatitis herpetiformis, pityriasis rubra (Hebra), mycosis fungoides, leukemia cutis, Hodgkin's disease involving the skin and arsphenamine dermatitis. Recently Sulzberger and Garbe [2] described a generalized eruption which they designated chronic discoid lichenoid dermatitis; and still more recently Cannon [3] reported on a group of patients with an erythroderma which he called allergic eczema. We believe that some of the latter patients

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1. Symmers, D.: Giant Follicular Lymphadenopathy With or Without Splenomegaly, Arch. Path. **26**:603 (Sept.) 1938.

2. Sulzberger, M. B., and Garbe, W.: Nine Cases of Distinctive Discoid and Lichenoid Dermatosis, Arch. Dermat. & Syph. **36**:247 (Aug.) 1937.

3. Cannon, A. B.: Allergic Dermatitis Simulating Lymphoblastoma, Arch. Dermat. & Syph. **39**:846 (May) 1939.

presented, in addition to the cutaneous lesions, giant follicular lymphadenopathy or its polymorphous cell sarcoma derivative, or both.

A study of the lymph nodes of 5 of our 15 patients showed transformation of giant follicular lymphadenopathy into polymorphous cell sarcoma of the lymph follicles; that of the remaining 10 showed simple giant follicular lymphadenopathy.

It is of interest from the standpoint of industrial medicine that several of our patients gave a history of an intractable dermatitis of the hands following some contact irritant. Either spontaneously or as the result of injudicious therapy the eruption had gradually become universal and associated with a persistent or remittent, lichenified, scaling dermatitis. A patient with this condition on removal from home or occupational environment, especially if moved to a warm dry climate, almost invariably experienced a temporary remission. Many patients improved after short periods of hospitalization without therapy, while others showed temporary improvement following induced hyperpyrexia. In a few treatment was of no avail, the giant follicular lymphadenopathy constituting apparently a preceding stage of a polymorphous cell sarcoma, Hodgkin's disease or lymphatic leukemia, as has been described by Symmers.

REVIEW OF THE LITERATURE

The first case of giant follicular lymphadenopathy was reported in 1901 by Becker.[4] The patient was a woman aged 33 whose illness commenced with swelling of the cervical lymph nodes. During the subsequent three months all the superficial lymph nodes were involved. The spleen was massively enlarged. A node removed three years after the onset of the disease showed simple hyperplasia. Similar cases have been reported by Foix and Roemmele.[5] It was not until 1925, however, that the first report appeared in the American literaure. In that year Brill, Baehr and Rosenthal,[6] under the title of generalized giant lymph follicle hyperplasia of the lymph nodes and spleen, described 2 cases of a condition that was clinically and histologically almost identical with that in the case previously described by Becker. Both patients showed generalized lymphadenopathy due to numerical and dimensional hyper-

4. Becker, E.: Ein Beitrag zur Lehre von den Lymphomen, Deutsche. med. Wchnschr. **27**:726, 1901.

5. Foix, C., and Roemmele, A.: Contribution à l'étude du sarcome primitif de la rate à propos d'une forme spéciale, le réticulosplénome nodulaire, Arch. de méd. expér. et d'anat. path. **24**:111, 1912.

6. Brill, N. E.; Baehr, G., and Rosenthal, N.: Generalized Giant Lymph Follicle Hyperplasia of Lymph Nodes and Spleen, J. A. M. A. **84**:668 (Feb. 28) 1925.

plasia of the lymph follicles. The authors emphasized the clinical importance of the disease and the response to roentgen ray therapy.

In 1927 Symmers [7] reported 3 cases. Up to this time this entity had been considered benign. However, almost simultaneously Baehr and Rosenthal [8] revised their original opinion regarding the benignity of the disease, referring to it as malignant lymph follicle hyperplasia. Four years later Baehr, Klemperer and Rosenthal [9] stated that the entire process was a variety of lymphosarcoma and possibly might form a connecting link between systemic hyperplasia of the lymphatic tissue and lymphosarcomatosis. They suggested the name follicular lymphoblastoma. This interpretation was reiterated by Baehr,[10] who expressed the conviction that all cases of giant follicular hyperplasia are primarily instances of lymphosarcoma.

Subsequently Symmers reported on 26 new patients, 7 with a simple giant follicular lymphadenopathy, 7 with direct transformation of follicular lymphadenopathy into polymorphous cell sarcoma of the hyperplastic lymph follicles, 7 with lymphadenopathy associated with Hodgkin's disease and 4 with associated lymphatic leukemia. In another case necropsy showed necrotic folliculitis of the lymph nodes associated with giant follicular lymphadenopathy.

CLINICAL CONSIDERATIONS

Seventy-two cases of this condition have been reported in the literature. To this number we wish to add 15 cases. Unlike ours, in all of which cutaneous manifestations were exhibited, in most of the recorded cases there were changes confined to the lymphoid system.

Fourteen of our patients were males; the youngest was 15 years of age and the oldest 80. In only 2 patients did the cutaneous manifestations appear before the age of 30. The average age was 55.6 years. The average age of the patients seen by other observers was 39.3 years, the oldest being 77 and the youngest 2 years. Nine of the reported patients were less than 30. Forty-seven were males and 25 females. The disease is far more prevalent in men.

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7. Symmers, D.: Follicular Lymphadenopathy with Splenomegaly, Arch. Path. **3**:816 (May) 1927.

8. Baehr, G., and Rosenthal, N.: Malignant Lymph Follicle Hyperplasia of Spleen and Lymph Nodes, Am. J. Path. **3**:550 (Oct.) 1927.

9. Baehr, G.; Klemperer, P., and Rosenthal, N.: Follicular Lymphoblastoma (Giant Follicular Hyperplasia of the Lymph Nodes and Spleen), Am. J. Path. **7**: 558 (Oct.) 1931.

10. Baehr, G.: The Clinical and Pathological Picture of Follicular Lymphoblastoma, Tr. A. Am. Physicians **47**:330, 1932.

In our series 6 patients were Jewish, 3 Irish, 2 Chinese, 2 Italian, 1 Turkish and 1 French Canadian. There were no Negroes. The table gives a complete summary of the data.

The initial objective symptoms occurred either in the superficial lymph nodes or on the skin. From none of our patients, all of whom presented cutaneous lesions, was it possible to elicit a history of preceding lymph node enlargement. The nodes were discrete, movable

Tabulation of Patients with Giant Follicular Lymphadenopathy

Patient	Age	Sex	Clinical Features	Blood Examination	Duration	Termination
J. C.	65	Male	Pruritus; adenopathy; seborrheic eczema	—	1 mo.	?
S. F.	57	Male	Pruritus; erythema; cold feeling; adenopathy; exfoliative dermatitis	17% eosinophils	5 mo.	?
A. W.	80	Male	Pruritus; herpes zoster; exfoliative dermatitis; adenopathy	5% eosinophils; 3,800,000 R.B.C.	1 yr.	Polymorphous cell sarcoma
J. McM.	48	Male	Pruritus; adenopathy; discoid and lichenoid dermatitis	6% eosinophils	2 yr.	?
T. G.	31	Male	Adenopathy; pruritus; herpes zoster; exfoliative dermatitis	7% eosinophils; 3,100,000 R.B.C.	2 yr.	Polymorphous cell sarcoma; death
W. C.	57	Male	Pruritus; discoid and lichenoid dermatitis	12% eosinophils	2 yr.	?
M. A.	76	Male	Pruritus; exfoliative dermatitis	5% eosinophils; 3,900,000 R.B.C.	7 yr.	?
T. S.	68	Male	Pruritus; "allergic eczema"	.....	8 yr.	?
J. V.	75	Male	Pruritus; "allergic eczema"	3,600,000 R.B.C.	4 mo.	?
T. L.	66	Male	Pruritus; exfoliative dermatitis	7% eosinophils	3 yr.	Polymorphous cell sarcoma; death
S. Y.	17	Male	Pruritus; discoid lichenoid dermatitis	11% eosinophils	2 yr.	?
G. C.	56	Male	Pruritus; discoid lichenoid dermatitis	3% eosinophils	1 yr.	Polymorphous cell sarcoma; death
S. G.	54	Female	Pruritus; exfoliative dermatitis	.....	5 yr.	?
C. G.	30	Male	Pruritus; exfoliative dermatitis	4,000,000 R.B.C.	6 yr.	?
J. V.	56	Male	Mycosis fungoides	4% eosinophils	2 yr.	Polymorphous cell sarcoma; death

and painless, varying from 1 to 7 cm. in diameter. Clinically, this condition is almost always mistaken for Hodgkin's disease. Usually only the superficial nodes are involved (Symmers [1]), although Baggenstoss and Heck [11] reported cases in which the mesenteric nodes were apparently affected first. In occasional instances there is spontaneous diminution in size or complete regression of the lymph nodes. In

11. Baggenstoss, A. H., and Heck, F. J.: Follicular Lymphoblastoma (Giant Lymph Follicle Hyperplasia of Lymph Nodes and Spleen), Am. J. M. Sc. **200**:17 (July) 1940.

60 per cent of the cases reported there was enlargement of the spleen. In none of our cases was the spleen palpable.

Many of our patients suffered from anemia. It was usually mild and of the hypochromic variety. Studies of blood smears showed eosinophilia in 9 of the 15 cases, with the eosinophils ranging from 3 to 17 per cent. Mild leukopenia was often noted, the white blood cell count varying between 3,000 and 5,000.

PROGNOSIS

Giant follicular lymphadenopathy offers a favorable prognosis. It may respond to roentgen ray therapy. Unfortunately, after repeated irradiations its response is less spectacular, and some patients who initially showed improvement failed to react favorably. When the disease has undergone transformation into the polymorphous cell sarcoma, radiation therapy is less readily effective.[12]

REPORT OF CASES

In our patients who during the last two years were hospitalized we have observed three distinct types of cutaneous clinical pictures: first, the allergic eczema described by Cannon, including exfoliative dermatitis; second, a condition resembling that described by Sulzberger and Garbe as chronic discoid lichenoid dermatitis, and, third, the condition diagnosed clinically as mycosis fungoides. We have selected 1 patient to represent each type.

CASE 1.—*Erythroderma associated with giant follicular lymphadenopathy.*

C. G., a Jew aged 31, born in Poland, was admitted to Bellevue Hospital because of an intensely pruritic, erythematous, oozing, generalized eruption of two days' duration. Its onset had been sudden and was initiated by chills and profuse sweating while the patient was at work (as an operator on leather goods).

As a child his health had been good except that he had scrofula at the age of 5 years and pneumonia at the age of 13. His first eruption occurred at the age of 22 and consisted of a generalized dermatitis beginning in the popliteal regions and accompanied by intense edema of the face and scrotum. This responded to local therapy after several months. At this time he was employed as a fruit and vegetable peddler. He remained well for approximately six years, and then recurrent erythematous itching plaques developed on the extremities, for which he was treated with sulfur. As a result a generalized sulfur dermatitis developed, which regressed under soothing applications, only to recur with greater intensity.

On admission to the hospital the patient's physical condition was essentially normal except for generalized lymphadenopathy and erythroderma. His entire integument, including the scalp, was thickened, dusky red and covered with a flaky, loosely adherent, yellowish brown scale. At the flexures there was some infiltration and fissuring.

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12. Rubenfeld, S.: Radiation Treatment of Giant Follicular Lymphadenopathy and Its Polymorphous Cell Sarcoma Derivative (Symmers' Disease), Am. J. Roentgenol. **44**:875 (Dec.) 1940.

Examination of the blood showed a secondary anemia with 3 per cent eosinophils. The Wassermann reaction of the blood was negative. Roentgenograms of the chest were normal. Examination of the urine showed no arsenic. Scrapings from the skin showed no fungi. Since no clear area of skin was available, patch tests with leather could not be made. Microscopic examination of a superficial lymph

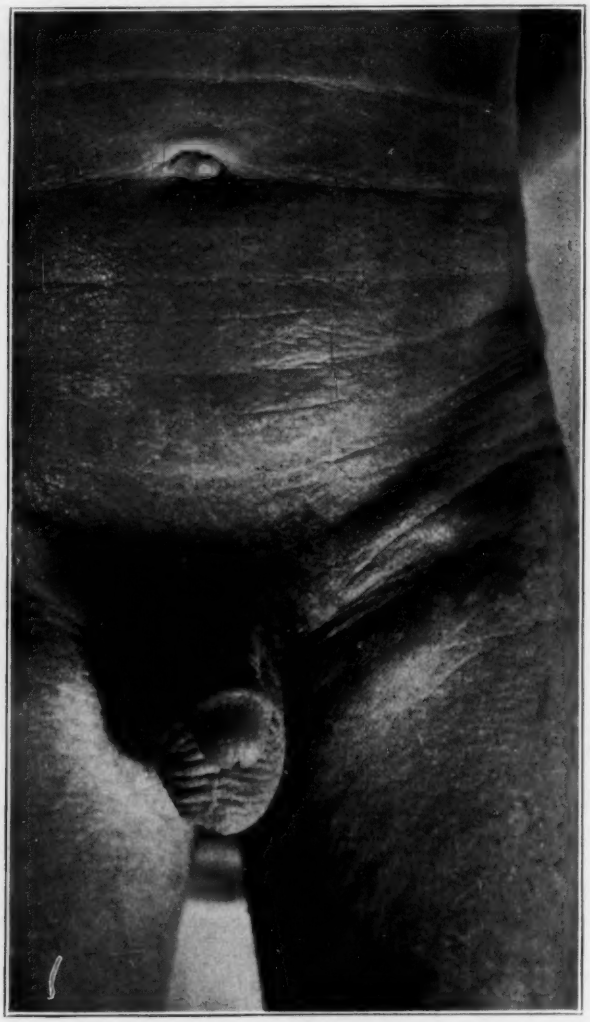

Fig. 1.—Erythroderma associated with giant follicular lymphadenopathy.

node showed the dimensional and numerical hyperplasia of giant follicular lymphadenopathy.

Sulzberger and Garbe have recently reported 9 cases of a discoid and lichenoid chronic dermatitis of unknown origin, characterized by pruritus and exudation with subsequent lichenification. They suggested that the condition might represent a premycosis, although other con-

siderations led them to suggest the possibility of a sensitization dermatitis. They, too, noted the beneficial effects of environmental changes in many of their patients. Other prominent features included eosinophilia, negative reactions to patch tests, absence of fungi on the skin, lack of intensification of the process after the administration of iodides, generalized lymphadenopathy and absence of a palpable spleen.

CASE 2.—*Chronic discoid lichenoid dermatitis associated with giant follicular lymphadenopathy.*

S. Y., a youth aged 17, was admitted to Bellevue Hospital with a discoid lichenoid dermatitis. His previous history was irrelevant. The eruption had begun two years previously on his arms and consisted of groups of intensely itching small follicular papules which later, owing to scratching, became universal. At various

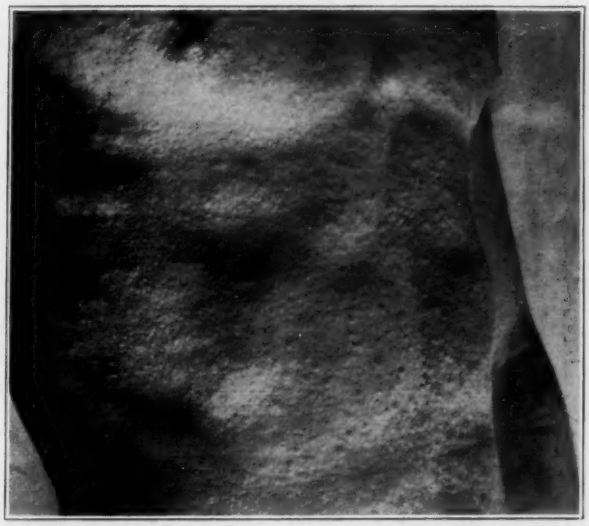

Fig. 2.—Chronic discoid lichenoid dermatitis associated with giant follicular lymphadenopathy.

times he was treated for scabies, lichen planus and arsenical dermatitis (after the injection of mercury salicylarsenate). Only for one short period was his skin clear.

Physically he was well developed and not acutely ill. Except for the eruption examination showed no abnormalities. The spleen was not palpable. His skin showed universal lichenification with a generalized discoid papular eruption, excluding the face. There were some scaling, some isolated areas of crusting and some profuse exfoliation.

Cytologic examination of the blood did not show any anemia but did show on one occasion 11 per cent eosinophils and on another occasion 16 per cent eosinophils. The Wassermann reaction of the blood was negative. Tests for fungi gave negative results. Roentgenograms of the chest were normal. Examination of the urine showed no arsenic. Microscopic examination of tissue taken from the skin showed a thin layer of keratin covering a hyperplastic layer of squamous epithelium. There was acanthosis, with the interpapillary processes extending into the underlying cutis. In the papillary layer there was a diffuse but moderate infiltration consisting of a

moderate number of small round cells, a few plasma cells and an occasional eosinophil. The interpretation was chronic dermatitis. One of the cervical lymph nodes showed changes previously described as in giant follicular lymphadenopathy.

CASE 3.—*Mycosis fungoides associated with giant follicular lymphadenopathy.*

J. J. V., a man aged 57, a French Canadian by birth, was admitted to Bellevue Hospital with the clinical diagnosis of mycosis fungoides. His previous and family

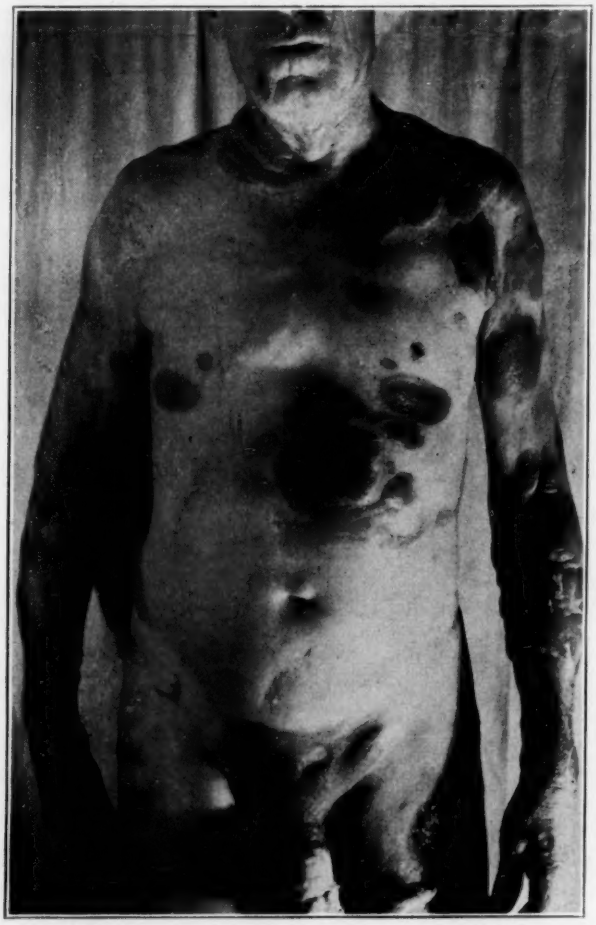

Fig. 3.—Mycosis fungoides associated with giant follicular lymphadenopathy.

histories were essentially negative. He stated that the eruption began two years previously as an erythematous patch on the left arm. This increased in size, extended over the entire extremity and subsequently spread to his trunk. The initial lesion on his left arm had been diagnosed as psoriasis, but no treatment was administered prior to his admission to the hospital. About two months before we saw him the lesions became infiltrated and began to fungate. In contrast to our other patients, pruritus was not a prominent symptom.

Physical examination showed no abnormalities except generalized lymphadenopathy and the eruption. The spleen was not palpable. The cutaneous lesions consisted of discrete, irregularly oval, discoid, fungating, granulomatous tumors on the trunk, extremities and penis. The surface of some of the lesions was terraced and bathed in a thin serous exudate.

Histologic examination of a lymph node showed giant follicular hyperplasia associated with changes suggestive of transformation into polymorphous cell sarcoma. The cortex contained enlarged and numerous germinal centers. The urine was normal, and the Wassermann reaction of the blood was negative. Examination of the blood showed: 4,030,000 erythrocytes and 9,700 leukocytes per cubic millimeter, 106 per cent hemoglobin, 4 per cent eosinophils, a color index of 1.2 and 32 mg. of nonprotein nitrogen, 1.5 mg. of creatinine and 65 mg. of dextrose per hundred cubic centimeters.

PATHOLOGIC CONSIDERATIONS

Pathogenesis.—Any attempt to explain the cause of giant follicular lymphadenopathy must of necessity be hypothetic. Its conception is probably due to contact with some endogenous or exogenous irritant or toxin capable of producing a variety of cutaneous changes associated with pruritus followed by secondary infection and attended or preceded by lymphadenopathy. If the patient is removed to another climate or avoids contact with substances responsible for his dermatitis he almost invariably improves. Both the skin and the lymph nodes may partake in this remission. We have noted in a few cases in which the condition was due to contact that continuation of exposure has resulted in the subsequent development of polymorphous cell sarcoma of the lymph follicles.

Histologically, according to Symmers,[1] the lymph nodes show replacement of their normal architecture by dimensional and numerical hyperplasia of the lymph follicles—giant follicular lymphadenopathy. The cases are separable into two groups. In the first group are those in which the hyperplastic lymph follicles maintain their structural integrity for months or years, or the nodes may undergo reduction in size and even disappear or show signs of healing, as evidenced by patches of granulation tissue, interfollicular connective tissue overgrowth and sclerotic follicles. In the second group are those in which the condition alters its course. In this group Symmers showed that (*a*) the hyperplastic lymphoid follicles may undergo direct transformation into a polymorphous cell sarcoma (this happened in 5 of our cases); (*b*) the lesion may show the histologic changes of Hodgkin's disease; (*c*) the lesion may show the changes of lymphatic leukemia, or (*d*) the lesion may become associated with necrotic folliculitis of the lymph nodes and spleen. In still other instances the combination of giant follicular lymphadenopathy, poly-

morphous cell sarcoma and Hodgkin's disease may be observed in the same lymph node.

Histologic Observations.—According to Symmers [1] also, the enlargement of the lymph nodes is due to numerical and dimensional hyperplasia of the lymph follicles. Lymph cords and sinuses are almost always obliterated. With few exceptions, every follicle is delimited by a zone of closely set, deeply staining small lymphocytes, laid down in one or more rows arranged in orderly sequence and fading gradually into the loosely distributed small lymphocytes of the parenchyma. The lymph follicles differ in size and shape. Many are massive; others are enlarged in varying proportions, and still others are diminutive. For the greater part, the follicles are round or oval, but in many instances they are fused to form large masses of different shapes. They may be so closely packed as to occupy almost all of the substance of the node, or they may be set apart at variable distances, the intervening areas consisting of small lymphocytes or fibrosis. The germinal areas vary in their staining qualities. Some of them stain lightly. These are composed for the major part of large embryonal follicular cells which are so poor in chromatin as to appear as shadow forms. Other follicles stain more deeply, being composed of the smaller embryonal follicular cells of the large lymphocytic type, the nuclei of which are relatively rich in chromatin. In the greater number of follicles there is an admixture of the two main varieties, but transitional forms may enter into the histologic picture. The latter are about midway in size between the two main varieties, and their nuclei are often indented or otherwise apparently deformed. They contain chromatin noticeably in excess of that of the large shadow-like hypochromatic cells and are traceable into the comparatively richly chromatic rounded or oval cells of the large lymphocytic type. In those instances in which giant follicular lymphadenopathy occurs alone or in the form of its polymorphous cell sarcoma derivative, or both, in association with dermatitis exfoliativa, the lymph nodes almost always show deposits of melanin.

SUMMARY AND CONCLUSIONS

A series of 15 cases of giant follicular lymphadenopathy, with or without its polymorphous cell sarcoma derivative, are reviewed, in which various clinical diagnoses, including allergic eczema, dermatitis exfoliativa (Wilson and Brocq), chronic discoid lichenoid dermatitis (Sulzberger and Garbe) and mycosis fungoides, had been made. It is recommended that all patients exhibiting chronic eczematoid dermatitis with lymphadenopathy have histologic studies made of the lymph nodes (preferably those in the cervical region), as this syndrome in its early stages is amenable to radiation therapy.

Furthermore, in event of a diagnosis of this condition, unless the patient is removed from the customary environment, the process may eventuate in a polymorphous cell sarcoma, Hodgkin's disease or lymphatic leukemia. In our series polymorphous cell sarcoma was known to have developed in 5 patients. In 4 of these the disease terminated fatally. It was impossible to trace the other 10 patients.

It is appreciated that our experience has been limited and that two years is too brief a period to follow such patients and to arrive at definite conclusions. However, it is hoped that this preliminary report may encourage further study of this type of lymphadenopathy in its relation to diseases of the skin.

ONYCHOMYCOSIS DUE TO ASPERGILLUS FLAVUS

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Organisms of the aspergillus group are generally regarded as saprophytes. Under certain conditions, however, they may acquire pathogenic properties and become capable of infecting the ear, lung and other parts of the body. There are a few recorded instances of diseased nails attributed to various types of aspergilli or related fungi.[1] In general, claims for such a relation have been vigorously criticized. Thom and Church [2] stressed the difficulties in interpreting the data furnished in the literature, especially since few investigators had carefully identified their cultures. In addition, clinical information was often lacking or fragmentary. In the rare cases in which such details were supplied,[3] the clinical picture seemed to resemble closely that seen in ordinary yeast infections of the nails and surrounding tissue (for example, paronychia), and it is not surprising therefore that some of the observers considered the aspergillus merely as a secondary invader. These data explain the current general skepticism toward reports in which this organism has been claimed as the cause of alterations in nails.

The condition in the case which we are reporting differed clinically and mycologically from those previously described. It represents, so far as we can ascertain, the first example of ungual disease caused by Aspergillus flavus. It is our belief that the evidence indicates, beyond a reasonable doubt, that this organism was the cause of the altered nail plate of the right large toe in our patient.

From the Department of Dermatology (service of Dr. Fred Wise), Montefiore Hospital for Chronic Diseases, New York.

1. (*a*) Emile-Weil, and Gaudin, L.: Onychomycoses causeés par Sterigmatocystis unguis, Arch. de méd. expér. et d'anat. path. **28**:465, 1919. (*b*) Sartory, A.: Sur un champignon nouveau du genre Aspergillus isolé dans un cas d'onychomycose, Compt. rend. Acad. d. sc. **170**:523, 1920. (*c*) Ota, M.: Sur une nouvelle espèce d'aspergillus pathogène: Aspergillus Jeanselmei, Ann. de parasitol. **1**:137, 1923. (*d*) Sartory, A.; Sartory, R.; Hufschmitt, G., and Meyer, J.: Un cas d'onychomycose provoquée par un Eurotium nouveau: Eurotium diplocyste n. sp., Compt. rend. Soc. de biol. **104**:881, 1930. (*e*) Smith, L. M.: Aspergillus Infection of the Nails, Urol. & Cutan. Rev. **38**:783, 1934.

2. Thom, C., and Church, M. B.: The Aspergilli, Baltimore, Williams & Wilkins Company, 1926.

3. Ota.[1c] Sartory.[1d] Smith.[1e]

REPORT OF A CASE

A woman 30 years old was observed for chronic bilateral fibrocavitary pulmonary tuberculosis and tuberculosis of the larynx. Tubercle bacilli were found in the sputum on a number of occasions. She complained incidentally of a deformed nail of the right big toe. This condition had been first noted by the patient about two years before admission, when it appeared as a dark spot on the proximal half of the nail. No alteration in the structure of the nail occurred until about a year later, the discolored area remaining more or less confined to its original site.

On examination the proximal part of the nail showed a dull green discoloration which seemed to be embedded in the depth and which extended to the lunula; the distal end of the nail was crumbling and fragmented (fig. 1).

Specimens of the nail were inoculated in Sabouraud's medium and in corn meal agar. Within three days both mediums showed yellow colonies that became

Fig. 1.—Nail infected with A. flavus. Arrow points to the area of greenish discoloration in the proximal part. The distal part is crumbling and fragmented. The remaining toe nails are unaffected.

green in the next twenty-four to forty-eight hours, the growth being more rapid on Sabouraud's medium. This organism, tentatively identified as an aspergillus, was considered a probable contaminant in view of the prevalent belief that such fungi are merely saprophytes, especially in the nails. A second culture on Sabouraud's medium again revealed the same organism. On the third occasion the fungus was again isolated from this toe, whereas all the other toes of the same and of the other foot yielded sterile cultures. A specimen of the growth was identified by Dr. F. Weidman as an aspergillus, and as the organism seemed to be an unusual one, Dr. Weidman advised sending a specimen to Dr. C. Thom, of the Department of Agriculture, for a more detailed identification. Dr. Thom found that the culture had "the structure of A. flavus" and stated, furthermore, that he had seen this strain but once before. Up to this time several direct examinations of the distal fragments of the nail had shown no mycelium or other

evidence of direct invasion of the nail substance. In view of the peculiar appearance of the discoloration and its location in the proximal part of the nail, the question arose of whether the crumbling might be due to an incidental involvement of the matrix with secondary dystrophic changes.

The patient was treated for three months with topical applications of 10 per cent ammoniated mercury, and later the affected nail received in all 250 r of unfiltered roentgen rays. These measures produced no visible evidence of improvement. At the end of this period the culture was repeated, and again the same organism was recovered. It may be mentioned that all four times cultures of the fungus were pure, without any contamination. A section of the fragmented portion of the nail plate, stained with hematoxylin and eosin, failed to disclose mycelium. In the meantime, additional information on the nature of the organism and the clinical features of the case having been acquired, it was decided to repeat the direct examination of the nail. This time, however, deeper portions of the nail plate, near the proximal discolored area, were taken for examination after preliminary shaving of the top layers of the nail, and now there was revealed an abundance of branching, septate hyphae in the deeper parts with groups of spores in the more superficial areas. As will be seen later, this correlated well with the appearance in the cultures. The technic for the direct examination of the nail plate was the usual one involving the use of 20 per cent potassium hydroxide and mild heating for about a minute. In view of the nature of the infection and the clinical course, it became clear why treatment with topical remedies and roentgen irradiation was likely to fail. It seems probable that removal of the entire nail surgically will be essential for cure. The latter procedure has not been recommended thus far, owing to the serious general state of the patient.

A. FLAVUS

General Data.—A. flavus is commonly found in the soil and in cereals.[4] It has been known since 1882 [5] as a fairly frequent cause of aspergillosis of the ear. The organism has apparently never been found in pulmonary aspergillosis. Our case is the first one in which A. flavus has been identified definitely in connection with ungual disease. We are unable to furnish precise information as to the source of the particular strain found in our patient. The ears were normal, and, while it is true that pulmonary tuberculosis may complicate aspergillosis of the lungs, this part of the body seemed an unlikely site for the primary source, when one considers the rarity of A. flavus in pulmonary infections.

Gross Cultural Characteristics.—Our description is based entirely on the behavior of this organism on Sabouraud's medium as observed by us. Specimens of the affected nail yielded no growth until three or four days had elapsed. Within twenty-four hours after its appearance there was observed a small grayish translucent spot just beneath the surface

4. Brumpt, E.: Précis de parasitologia, ed. 5, Paris, Masson et Cie, 1936, vol. 2, p. 1973.

5. Siebenmann, F.: Die Fadenpilze Aspergillus flavus, niger und fumigatus; Euroticum repens (und Aspergillus glaucus) und ihre Beziehungen zur Otomycosis aspergillina, Ztschr. f. Ohrenh. **12**:124, 1882-1883.

composed of fine lines radiating peripherally. In the center of this area there soon appeared a small collection of yellow powdery material which at first was only slightly elevated above the surface. In forty-eight to seventy-two hours the yellow became pale green as the colony increased in size, the green powdery center becoming more elevated and spreading centrifugally to cover the grayish translucent periphery (fig. 2). Subcultures generally grew more rapidly, the growth becoming manifest within twenty-four hours after the implantation. Growth on corn meal agar was slower and not as luxuriant.

Microscopic Cultural Appearance.—Through the cooperation of Dr. Michael Levine we were able to obtain a section of the culture in situ.

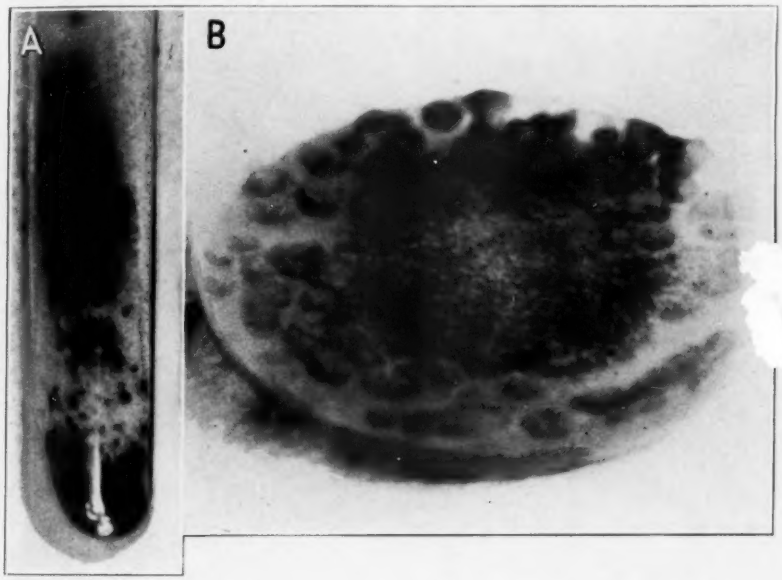

Fig. 2.—Appearance of A. flavus (*A*) after three days of growth on Sabouraud's medium (slant) and (*B*) after two weeks of growth on Sabouraud's medium.

A triangular piece of the culture, including the depth of the medium itself, was fixed, embedded and stained according to routine histologic technic. Examination of figure 3 shows branching septate hyphae just below the surface of the medium, whereas the aerial growth is composed of conidiophores terminating in balloon-like vesicles. Along the circumference of the vesicles are numerous sterigmata arranged in a single file. The sterigmata in turn give issue to straight lines of spores or conidia. The spores are responsible for the color of the colony [2] and also of the lesion itself. It is likely that the transparent appearance of the subsurface growth, as seen in the initial stages, is due to the mycelium.

Guinea Pig Inoculations.—An attempt was made to infect the skin and claws of a 2 month old guinea pig. Accordingly, pure specimens of the growth were placed on sandpaper and rubbed into the shaved skin of the back and into the claws of the right hind foot. Within forty-eight hours the skin of the back showed a scarified appearance with

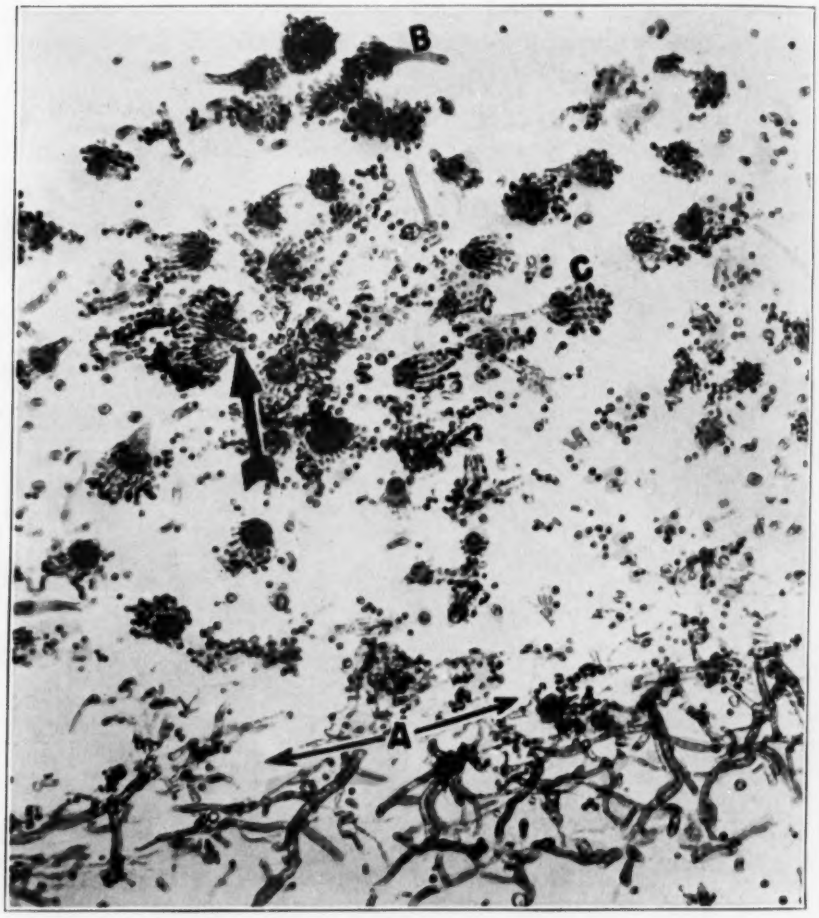

Fig. 3.—Microscopic cultural appearance of A. flavus. *A* indicates the level of the surface. Just below the surface the hyphae are seen in abundance. *B* shows a conidiophore ending in a balloon-like vesicle, seen best at the point of the arrow. The circumference of the vesicle shows a single file of sterigmata, from which straight lines of spores or conidia issue (*C*).

grayish and hemorrhagic crusts. Within the first week several cultures of the organism were obtained from both the inoculated skin and the claws, but thereafter the cultures remained sterile. At no time was there observed definite clinical evidence of mycotic infection of these areas, and

examination of the scrapings likewise gave negative results. The first few positive cultures can be explained best on the basis of spores becoming adherent to the inoculated sites. Consequently, we were unable to infect the skin and claws of a 2 month old guinea pig.

SUMMARY AND CONCLUSIONS

We are recording what seems to be the first instance of onychomycosis due to A. flavus. In this case the peculiar clinical appearance could be correlated with the nature of the growth, the discoloration of the nail being due probably to the spores of the organism. The data compiled in this study indicate, beyond a reasonable doubt, that A. flavus was the cause of the ungual condition. The evidence for this belief is: (1) the unusual clinical appearance of the proximal portion of the affected nail, featured by a greenish discoloration within the nail plate itself; (2) the repeated isolation of the same organism in pure culture from the affected nail and failure to cultivate it from the nails of the remaining toes; (3) the isolation of A. flavus after several months of varied treatments; (4) the presence of mycelium in the deeper part of the discolored nail plate with spores in the more superficial portions, and (5) the rarity of the organism, so far as cultures of the nails are concerned, and the rarity of the particular strain isolated. We regard these data as reasonable evidence of cause and effect, despite the failure to fulfil Koch's postulates. This is a requirement that in our opinion presents enormous difficulties of fulfilment in infections of the type described.

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ONYCHOLYSIS IN FUR WORKERS

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Onycholysis, generally considered an uncommon disease of the finger nails, was found with a high degree of frequency in fur fleshers in the course of a study of the fur industry recently completed by the Division of Industrial Hygiene of the New York State Department of Labor. This finding is believed to be of sufficient interest to warrant a separate report.

A review of the literature reveals that a number of cases of onycholysis have been reported from time to time; and in some of these the patient's occupational exposure was regarded as a causative factor. Harris,[1] in a report of a study of fur workers, said that "the nails of dyers frequently showed considerable separation from the matrix, and were thick and ridged." In their recent textbook on occupational diseases of the skin, Schwartz and Tulipan [2] wrote, "During the busy season fleshers have their finger nails worn down to the quick as a result of friction from pulling the skins over the fleshing knife." These authors also listed cases of onycholysis in bartenders, bottle washers, cigar makers, confectioners, farm laborers, fruit workers, gardeners, milkers, vegetable cleaners and washerwomen. Klebanov and Emdin [3] reported onycholysis associated with cutaneous ulceration among wet leather strippers. The occupation of these persons was apparently similar to that of the fur fleshers herein reported. Neugebauer [4] described the condition in a washerwoman and ascribed it to the strong

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1. Harris, L. I.: A Clinical and Sanitary Study of the Fur and Hatters' Fur Trade, Monthly Bull. Dept. Health City New York, 1915, vol. 5, p. 267.

2. Schwartz, L., and Tulipan, L.: Occupational Diseases of the Skin, Philadelphia, Lea & Febiger, 1939, p. 279.

3. Klebanov, G., and Emdin, V.: Occupational Affections of the Nails in Leather Workers, Gig. truda, 1927, no. 5, p. 53; abstracted, J. Indust. Hyg. & Toxicol. **10**:195, 1928.

4. Neugebauer: Wien. klin. Wchnschr. **27**:39, 1914; cited by White, R. P.: The Dermatergoses, or Occupational Affections of the Skin, ed. 4, London, H. K. Lewis & Company, Ltd., 1934.

alkali in the soap. Templeton [5] found onycholysis frequently among girls who were employed in removing wetted paper labels from bottles. Viecelli [6] reported 1 case in which the patient was a hide worker. McRoberts [7] described a case of onycholysis in a nurse in whom the condition had developed from bathing patients.

In other reports nonoccupational causes, such as anemia, syphilis, eczema, psoriasis, tinea, hypothyroidism avitaminosis and congenital defects, were considered.[8] These causes were ruled out in our cases.

In the present study the finger nails of 91 fur fleshers were examined. These workers were engaged in separating the corium from the fur pelt. The pelts to be processed came to the fleshers steeped in brine in which the fur had been soaking. The hands of the workers were thus continually wet, resulting in maceration of the skin. Mechanical trauma was induced by the workers themselves who used their nails to aid in removing the corium from the pelts, although they were provided with suitable knives for the purpose. However, the fleshers found that using their own finger nails helped to speed up the process.

Onycholysis consists of a separation of the nail from the nail bed. The process begins at the distal nail margin and more or less gradually extends proximally to involve the entire nail. The involved nail is lost, and a new nail grows in normally. In some of the cases observed in this study the newly forming nail was also involved in the process of separation from its bed before it had had an apportunity to reach its full growth. In other workers erosion of nail plates in addition to onycholysis was seen. Two mechanisms appear to be involved, namely, maceration of the skin underlying the nail at its distal margin and mechanical trauma. None of the fleshers examined had an infection of the finger nails or dermatitis.

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5. Templeton, H. J.: Onycholysis: An Industrial Dermatosis, J. A. M. A. **97**:1950 (Dec. 26) 1931.

6. Viecelli, J. D.: Onycholysis, Arch. Dermat. & Syph. **33**:697 (April) 1936.

7. McRoberts, D. D.: Onycholysis: Report of a Case, Northwest Med. **39**:95, 1940.

8. Pardo-Castello, V.: Diseases of the Nails, Springfield, Ill., Charles C. Thomas, Publisher, 1936. Friedmann, M.: Ueber einige seltene Nagelerkrankungen, Arch. f. Dermat. u. Syph. **135**:161, 1921; cited by Pardo-Castello.[8] Fox, E. C.: Diseases of the Nails: Report of Cases of Onycholysis, Arch. Dermat. & Syph. **41**:98 (Jan.) 1940. Chargin, L.: Onycholysis Idiopathica, ibid. **21**:1051 (June) 1930. White, C. J.: A Clinical Study of Nail Diseases, Boston M. & S. J. **147**: 537, 1902. Crocker, H. R.: Diseases of the Skin, ed. 2, Philadelphia, P. Blakiston, Son & Co., 1903. Ingram: A Case of Onycholysis, Brit. J. Dermat. **44**:447, 1932. Strauss, M. J.: Onycholysis and Onychomadesis: Report of Case of Each with Review of Literature, Arch. Dermat. & Syph. **26**:644 (Oct.) 1932.

These workers did not complain of pain or of any other discomfort because of the nail separation. Some of the men offered the information, however, that on resuming work after a layoff of two to three weeks some small degree of pain was experienced. This, however, lasted only a few days. The condition does not seem to result in disability.

Detailed findings in the 91 fleshers whose nails were examined are presented in the table. It will be observed that 70 persons (76.9 per cent) were found to have some degree of onycholysis. No relation was found, however, between the degree of onycholysis and the length of continuous employment.

Incidence of Onycholysis in Ninety-One Fur Fleshers

Onycholysis	Number of Patients	Per Cent of Total
None	21	23.1
Some degree	70	76.9
One finger	14	15.4
Two fingers	11	12.1
Three fingers	12	13.1
More than three fingers	33	36.3

Prevention of onycholysis among fur fleshers is dependent on the use of tools instead of finger nails in the process of removing the corium from the fur pelt. Gloves are not feasible for this work because they materially impair efficiency.

CONCLUSIONS

Onycholysis is a relatively common but preventable condition among fur fleshers. It is disfiguring but not disabling. Two factors in the work appear to be responsible for its development: (1) maceration of the skin underlying the nail at its distal end and (2) mechanical trauma.

XCIII. SPECTROGRAPHIC ANALYSIS OF NEURODERMATITIC LESIONS

A HUMAN MAGNESIUM DEFICIENCY

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AND

MARTIN F. ENGMAN SR., M.D.

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In a preliminary report two of us (Engman and MacCardle [1]) described the mineral changes in the lesions of chronic disseminated neurodermatitis skin, which we believe is characterized by a localized magnesium deficiency. The study of the histologic features of this disease was published in a separate paper,[2] and we now wish to present a detailed account of the spectrographic analysis. Whether or not mineral changes occur in the development of a lesion of neurodermatitis has not been determined heretofore, largely because of the technical difficulties involved in detecting and measuring such minute quantities of an element as obtain in small biopsy specimens of skin. These obstacles can be partly overcome by use of a method of spectrographic analysis developed by McMillen and Scott [3] and since improved by Scott.

The primary shock tissue in neurodermatitis has never been determined definitely, and in view of the fundamental importance of ascertaining the focus of the earliest reaction to the causative agent, it

Dr. E. V. Cowdry and Dr. Gordon H. Scott assisted in this study, the latter having placed his equipment at our disposal.

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Studies, observations and reports from the Department of Dermatology of the Barnard Free Skin and Cancer Hospital and the Anatomical Laboratory of Washington University School of Medicine.

1. Engman, M. F., and MacCardle, R. C.: A Histochemical Study of Neurodermatitis: Preliminary Report; Microincineration and Spectrographic Analysis, Arch. Dermat. & Syph. **42**:109 (July) 1940.

2. MacCardle, R. C.; Engman, M. F., Jr., and Engman, M. F.: Histology of Neurodermatitis, to be published.

3. McMillen, J. H., and Scott, G. H.: An Interrupted Arc for Spectral Analyses, Rev. Scient. Instr. **8**:121, 1937.

was felt that a study of the minerals at various stages of the lesion would be of value. Alexander [4] and his followers have expressed the belief that by reason of the perivascular infiltration in neurodermatitis the capillary membrane is the locus of the earliest detectable lesion if not the primary reaction. Others (Bukovsky,[5] Vignolo-Lutati [6] and Wise [7]) have stated that the epidermis is the first to react. While the spectrographic analysis of whole skin does not afford a way of localizing the primary change, the relatively accurate quantitative estimation of a wide range of minerals is an invaluable aid in determining the topography of the primary mineral change by microincineration.

The relation of minerals to pigmentation and to keratinization is interesting. Keil and Nelson [8] noted that dark-coated rats made anemic by feeding on a copper-free diet underwent decided changes in pigmentation of hair. Black hair became light gray. Supplementing the diet with copper corrected this deficiency. The constitution of keratin deposits in the corneum evidently depends on the kinds of sulfhydril compounds available, for Klauder and Brown [9] found that the total sulfur of normal keratin is divided between cysteine and cystine, while Wilkerson and Tulane [10] found that the total sulfur of keratin in the corneum of exfoliative dermatitis skin is equally divided between cysteine and methionine. Melanin contains a considerable amount of sulfur in the form of glutathione and methionine, and it is conceivable that minerals, such as copper, may take an active catalytic part in the synthesis of cystine from methionine for keratinization. There is little or no melanin deposited in the epidermis of patients with exfoliative dermatitis, and it is likely that the methionine is not normally utilized but rather thrown off into the corneum, thus depriving the epidermal cells of an essential compound. Klauder and Brown [9] observed that in 2 cases of chronic disseminated neurodermatitis (a disease in which depigmentation is complete and the corneum hyperkeratinized) the sulfur content of the skin was increased, although they did not state the nature of the sulfur-containing compounds.

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4. Alexander, A.: Neurodermitis, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, vol. 6, p. 371.

5. Bukovsky, J.: Zur Frage der Neurodermitiden, Česká dermat. **3**:57, 1922.

6. Vignolo-Lutati, K.: Neurodermitis linearis psoriasiformis, Arch. f. Dermat. u. Syph. **111**:747, 1912.

7. Wise, F.: Pruritus with Lichenification, New York M. J. **118**:688, 1923.

8. Keil, H. I., and Nelson, V. E.: The Role of Copper in Hemoglobin Regeneration and in Reproduction, J. Biol. Chem. **93**:49, 1931.

9. Klauder, J. V., and Brown, H.: Certain Phases of Sulfur Metabolism of the Skin, Arch. Dermat. & Syph. **34**:568 (Oct.) 1936.

10. Wilkerson, V. A., and Tulane, V. J.: The Chemistry of Human Skin: III. The Occurrence of Methionine in Human Skin, J. Biol. Chem. **129**:477, 1939.

In neurodermatitis the epidermis is exceedingly acanthotic with many mitotically dividing cells at certain stages of the developing and healing lesions. There is no pigment deposited in the basal cells of such lesions, and the corneum is hyperkeratinized. Nothing is known of the relation between minerals and acanthosis in neurodermatitis, although many elements, such as sulfur, have been known to stimulate rapid growth of tissues.

Minerals of the human skin have not been extensively studied, although several different methods have been used and many isolated specimens studied. Brown [11] has published perhaps the best mineral analysis of a series of specimens of skin taken from cadavers. He made chemical analyses of the skin at different ages and determined its content of potassium, sodium, calcium, silicon, magnesium and phosphorus. Brown pointed out that there is a constantly changing mineral content of the skin and that there is no evidence of an age of chemical maturity such as Moulton [12] had reported for animals. Klose,[13] by chemical analysis, found considerable variation in the sodium, potassium and chlorine content of the skins of a few normal infants and of infants with nutritional disturbances. Klauder and Brown [9] found that the sulfur content of human skin decreases with age and increases in malignant melanomas. Cunningham [14] found copper in one specimen of human skin and in hair. Eggleton [15] stated that the zinc content of human epidermis probably represents that taken in with the food. He expressed the opinion that zinc is not an essential element.

Spectrographic analyses of human skin have been confined mostly to a few isolated pathologic specimens, and the analyses were made in most instances to detect injurious metals, such as lead, arsenic and gold. Sheldon and Ramage,[16] using the flame spectrum, found in the skin of a 24 week fetus rubidium, copper and manganese, in addition to the other well recognized essential elements of protoplasm. Gerlach and

11. Brown, H.: The Mineral Content of Human Skin, J. Biol. Chem. **75**:759, 1927.

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15. Eggleton, W. G. E.: The Zinc Content of Epidermal Structures, Chinese J. Physiol. **13**:399, 1938.

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Gerlach [17] have examined many specimens of normal and pathologic human skin and have discussed in detail argyria of the skin. Gaul and Staud [18] published a series of papers on the detection by spectrographic analysis of variously abnormally deposited elements, such as gold, silver, arsenic and lead. Okajima [19] analyzed several specimens of human pathologic tissues, including skin.

Scott and Williams,[20] using the recently improved high frequency current sparking device, reported the mineral content of several specimens of normal and pathologic human skin. They did not, however, study a series of specimens of human skin, being interested primarily in the perfection of the technic, which we used in the analyses to be reported. Cowdry, Heimberger and Williams [21] made spectrographic analyses of eight specimens of normal human skin from cadavers in connection with their study of leprous lesions, recording line densities for calcium, magnesium, phosphorus, iron and sodium.

MATERIALS AND METHODS

Since there are no published reports dealing with normal human skin studied in this way, we first undertook to establish an estimate of the minerals in normal tissue by a study of 83 specimens of skin taken for biopsy from normal persons varying in age from infancy to 91 years. The distribution of these specimens as to age and region of the body was given in our recent paper on the histology of neurodermatitis.[2]

Biopsy specimens from 33 patients with chronic disseminated neurodermatitis were taken chiefly from the cubital fossa and popliteal regions, where active lesions prevailed. In 22 of the cases specimens were removed also from the region of the midmaxillary line, where the skin seemed healthy, except for its typically

17. Gerlach, Walther, and Gerlach, Werner: Der Elementnachweis im Gewebe; zur Frage der Argyrosen, insbesondere über den spektrographischen Silbernachweis in der Haut, Dermat. Wchnschr. **95**:1497, 1932; Die chemische Emissionsspektralanalyse. Anwendung in Medizin, Chemie und Mineralogie, Leipzig, L. Voss, 1933.

18. Gaul, L. E., and Staud, A. H.: Clinical Spectroscopy: A Study of Biopsy Material Taken from Patients Receiving Gold Sodium Thiosulfate, Arch. Dermat. & Syph. **28**:790 (Dec.) 1933; Clinical Spectroscopy: A Study of Biopsy Material Taken from Patients Who Had Received Intravenous Injections of Silver Arsphenamine, ibid. **30**:433 (Sept.) 1934; Clinical Spectroscopy: Seventy Cases of Generalized Argyrosis Following Organic and Colloidal Silver Medication Including a Biospectrometric Analysis of Ten Cases, J. A. M. A. **104**:1387 (April 20) 1935.

19. Okajima, S.: Spectral Analysis of Metals: II. Spectroanalysis of Metals, Especially Heavy Metals in Pathological Human Tissues, Acta scholae med. univ. imp. in Kioto **14**:88, 1933.

20. Scott, G. H., and Williams, P. S.: The Spectrographic Analysis of Biological Materials, Anat. Rec. **64**:107, 1935.

21. Cowdry, E. V.; Heimberger, L. F., and Williams, P. S.: A Spectrographic Study of Leprous Lesions, Am. J. Path. **12**:13, 1935.

tough nature, and had never been affected by lesions of the disease. Specimens of healed neurodermatitic lesions were obtained from 6 patients whose active lesions had been previously studied histologically. As further controls, several other inflammatory cutaneous diseases, previously listed,[2] were similarly studied.

Sites for removal of biopsy material from diseased patients were treated with a 3 per cent mixture of boric acid in cold cream twice during the week previous to the time of the operation, in order to free the lesions from contaminant substances. Excision was done with a clean chromium-plated scalpel from the center of a large area washed with dehydrated alcohol and anesthetized by the intradermal injection of a 0.5 per cent aqueous solution of procaine hydrochloride (three to five minutes previous to removal of the specimen) into surrounding sites about 30 mm. distant from the points of biopsy (block anesthesia). Tests with rats showed that there are no appreciable differences in the spectrums of skin treated and not treated with procaine hydrochloride unless the removal of the biopsy specimen is delayed for at least thirty minutes after injection of the anesthetic. Furthermore, spectrums of specimens of human skin taken under general anesthesia do not differ from those removed under local anesthesia (with procaine hydrochloride).

With chromium-plated forceps, the excised specimens of skin were placed on pieces of clean filter paper, and the excess fat was removed with chromium-plated scissors. After as much blood as possible was blotted off, the specimens were cut into three parts, one for histologic study, one for microincineration and one for spectrographic analysis. Observations made by the method of microincineration will be reported in a later paper.

The pieces for spectrographic analysis were cut about 4 mm. square and were placed in mineral-free pyrex tubes. They were dissolved in nitric acid triply distilled in pyrex vessels, and the resultant souplike mixtures were dried on a roller carbon. The amounts of nitric acid as well as the sizes of the samples were approximately equal in all cases. These mixtures were then arced two hundred times on a sparking device, described by McMillen and Scott [3] and since improved by Scott, in front of a Bausch and Lomb medium quartz spectrograph. Spectrums were photographed on Eastman 50, 10 by 12 inch (25 by 30 cm.), spectrographic plates. Spectrums of specimens of neurodermatitis skin and of normal and pathologic control skins were usually photographed on the same plate, and the plate was developed in Eastman D61a solution at 55 F. for six minutes, according to Scott's routine procedure.

The intensities of the lines were read on a recording microphotometer in the physics department of Washington University by Mr. Otto J. Baltzer and later calculated by him, the experimental error being not more than 0.01. Only some of our spectrograms have been thus calculated (table). The remainder were sufficiently like those read and calculated to lead us to believe that their detailed examination would merely multiply figures without altering the conclusions to be reached.

A list of the spectrograms made is as follows: 83 of normal skin, 33 of active lesions of neurodermatitis, 22 of unaffected skin of patients with neurodermatitis, 6 of healed neurodermatitic lesions and 55 of control specimens of other cutaneous diseases.

Our results with the spectrograph were checked in the following way: Since it was not feasible to remove with the biopsy material a sufficient amount of skin for direct chemical analysis of magnesium, in which we were primarily interested, Dr. H. A. Bulger and Mrs. Olive O'Byrne made quantitative determinations of magnesium for us in ten samples of human blood serum.

Relative Intensities of Lines of Radiation on Spectrograms of Biopsy Specimens of Normal and of Pathologic Human Skin (Measured Microphotometrically)

	Specimen Number	Age of Patient, Years	Calcium	Copper	Magnesium	Iron	Phosphorus	Zinc
Normal skin	1	10	0.028	0.048	0.105	0.009	0.026	0.025
	2	14	0.033	0.118	0.059	0.013	0.028	0.018
	3	18	0.032	0.036	0.140	0.023	0.138	0.025
	4	6	0.045	0.049	0.121	0.006	0.002	0.022
	5	12	0.027	0.036	0.110	0.091	0.020	0.030
	6	20	0.020	0.119	0.084	0.025	0.016	0.030
	7	19	0.018	0.083	0.116	0.011	0.013	0.037
	8	29	0.020	0.118	0.186	0.023	0.020	0.036
	9	36	0.032	0.084	0.122	0.007	0.020	0.044
	10	24	0.012	0.140	0.300	0.120	0.015	0.037
	11	7	0.033	0.176	0.192	0.020	0.140	0.032
	12	16	0.045	0.104	0.256	0.032	0.025	0.028
	13	15	0.028	0.060	0.160	0.024	0.013	0.024
	14	18	0.032	0.066	0.300	0.054	0.130	0.028
	15	21	0.027	0.052	0.160	0.120	0.014	0.036
	16	13	0.020	0.112	0.104	0.020	0.028	0.036
	17	32	0.018	0.100	0.132	0.010	0.025	0.052
	18	26	0.011	0.200	0.190	0.108	0.016	0.025
	19	8	0.000	0.074	0.175	0.045	0.002	0.031
	20	14	0.000	0.065	0.179	0.047	0.026	0.036
	21	33	0.005	0.044	0.193	0.040	0.013	0.022
	22	22	0.015	0.180	0.300	0.250	0.020	0.026
	23	11	0.037	0.096	0.195	0.225	0.016	0.021
	24	14	0.005	0.072	0.110	0.055	0.028	0.040
Active neurodermatitic lesions	25	14	0.011	0.086	0.053	0.060	.....	0.027
	26	22	0.018	0.067	0.036	0.007	.....	0.036
	27	13	0.118	0.013	0.036	.....	.....	0.080
	28	17	0.037	0.010	0.043	.....	.....	0.014
	29 (61)	31	0.012	0.013	0.048	.....	.....	0.068
	30	5	0.030	0.021	0.048	.....	.....	0.018
	31 (59)	9	0.010	0.090	0.025	.....	.....	0.018
	32	24	0.018	0.086	0.036	0.007	.....	0.080
	33 (50 and 60)	18	0.010	0.034	0.054	.....	.....	0.015
	34	3	0.011	0.068	0.072	0.170	.....	0.027
	35	32	0.010	0.034	0.065	0.015	.....	0.030
	36 (51)	15	0.018	0.088	0.090	0.024	.....	0.040
	37	5	0.118	0.028	0.044	0.010	.....	0.028
	38 (52)	10	0.012	0.036	0.090	0.005	.....	0.028
	39	17	0.030	0.052	0.010	0.016	.....	0.030
	40	22	0.011	0.136	0.085	0.112	.....	0.044
	41 (56)	22	0.018	0.104	0.064	0.016	.....	0.040
	42	13	0.021	0.235	0.088	0.234	.....	0.027
	43 (58)	19	0.049	0.220	0.092	0.170	.....	0.029
	44	14	0.013	0.095	0.010	1.750	.....	0.035
	45	23	0.030	0.021	0.048	.....	.....	0.018
	46 (57)	24	0.010	0.090	0.025	.....	.....	0.018
	47 (54)	1¼	0.018	0.066	0.050	.....	.....	0.028
	48 (55)	19	0.036	0.104	0.065	.....	.....	0.030
	49 (53)	17	0.118	0.100	0.070	.....	.....	0.014
Unaffected neurodermatitis skin	50 (33 and 60)	18	0.044	0.078	0.053	0.100	.....	0.026
	51 (36)	15	0.048	0.025	0.091	0.040	.....	0.029
	52 (38)	10	0.000	0.040	0.055	0.023	.....	0.044
	53 (49)	17	0.040	0.092	0.025	.....	.....	0.044
	54 (47)	1¼	0.015	0.032	0.030	0.015	.....	0.020
	55 (48)	19	0.010	0.172	0.036	0.064	.....	0.028
	56 (41)	22	0.044	0.108	0.108	0.116	.....	0.046
	57 (46)	24	0.020	0.270	0.063	0.190	.....	0.025
	58 (43; a yr. later)	18	0.008	0.108	0.100	0.256	.....	0.031
	59 (31)	9	0.044	0.078	0.100	0.100	.....	0.026
Healed neurodermatitic lesions	60 (33 and 50)	18	0.048	0.070	0.090	0.200	.....	0.027
	61 (29)	31	0.195	0.028	0.040	0.250	.....	0.010
	62	22	0.049	0.070	0.080	0.180	.....	0.020
Infantile eczema	63	..	0.100	0.030	0.240	0.020	.....	0.024
Psoriasis	64	..	0.015	0.185	0.140	0.012	0.007	0.022
	65	..	0.015	0.220	0.192	0.024	.....	0.032
	66	..	0.012	0.144	0.188	0.016	.....	0.036
	67	..	0.026	0.109	0.170	0.300	.....	0.034
	68	..	0.045	0.430	0.113	0.063	.....	0.024

Relative Intensities of Lines of Radiation on Spectrograms of Biopsy Specimens of Normal and of Pathologic Human Skin (Measured Microphotometrically)—Continued

	Specimen Number	Age of Patient, Years	Calcium	Copper	Magnesium	Iron	Phosphorus	Zinc
Exfoliative dermatitis	69	..	0.118	0.064	0.105	0.005	0.011	0.023
Contact dermatitis	70	..	0.028	0.185	0.146	0.092	.....	0.050
	71	..	0.018	0.167	0.131	0.100	.....	0.038
	72	..	0.024	0.130	0.151	0.146	.....	0.030
Chronic dermatitis	73	..	0.005	0.116	0.230	0.272	.....	0.022
	74	..	0.005	0.094	0.192	0.156	.....	0.052
Xeroderma pigmentosum	75	..	0.017	0.131	0.100	0.011	.....	0.025
Senile keratosis	76	..	0.020	0.180	0.111	0.180	.....	0.036
Lichen planus	77	..	0.018	0.118	0.240	0.205	.....	0.028
Localized neurodermatitis	78	71	0.195	0.048	0.025	0.200	.....	0.028
	79	46	0.045	0.100	0.188	0.023	.....	0.022
	80	43	0.018	0.044	0.110	0.045	.....	0.037
	81	28	0.032	0.096	0.192	0.047	.....	0.026
	82	53	0.027	0.066	0.121	0.013	.....	0.040
	83	50	0.011	0.074	0.132	0.020	.....	0.032

The spectrographic and chemical determinations in blood serums of normal patients and of patients with neurodermatitis checked reasonably well, the chemical analysis indicating a low magnesium content in cases in which the spectral lines were less intense and a high magnesium content in cases in which the spectral lines were more intense. We feel certain that a comparable degree of accuracy would hold for the results of analysis of the skin by the spectrographic method. Further checks have frequently been made by Scott and his associates and by us, known amounts of solutions of metals of known concentrations being used for spectrographic anlaysis.

ACTIVE NEURODERMATITIC LESIONS

By a comparison of the intensities of the lines, as listed in the table, it will be seen that there is a decided reduction in magnesium in every specimen of an active neurodermatitic lesion. In normal skin there is a wide range of variation in the amount of magnesium, whereas in active lesions of neurodermatitis the amount of this element is relatively constant. This reduction in magnesium seems to be so consistent that it suggests a magnesium deficiency in the skin of patients with this disease. The serum magnesium of these patients is well within the normal range, as is also the calcium.

The calcium content of active lesions does not vary much from that of normal skin. It might be expected that the calcium content of the skin of such lesions would also either decrease or increase to compensate for such a loss of magnesium, but examination of the calcium lines does not reveal any such consistent adjustment. There seems to be no relation between the proportions of calcium and magnesium, for in cases of high magnesium values the calcium may be either high or low, as in specimens 39 and 44, and, conversely, in cases of high calcium values the magnesium may be high or low.

The only other consistent difference between normal skin and active lesions of neurodermatitis is in the phosphorus lines. In active lesions these lines are so faint that their relative intensities can scarcely be

calculated. However, this apparent lack of phosphorus is peculiar to active lesions not only of neurodermatitis but also of other diseases, such as psoriasis, in which the magnesium balance is undisturbed.

The iron content of active lesions does not vary consistently, although it may be noted that whenever iron is present in large amounts the magnesium value is also high. The excess of both magnesium and iron may in cases of this kind be accounted for by the presence of extravasated blood in the cutis (observed in the histologic sections). However, in cases of high magnesium and low iron values, the excess magnesium is not easily accounted for except that it was present in the epidermis. The white ash of calcium and magnesium in these cases will be described in a subsequent paper.

The copper lines in active lesions are usually slightly less intense than in any of the normal and pathologic controls, although in some cases they are more intense. In cases in which the iron lines are more intense, the copper lines are also usually more intense; although when copper lines are intense, the iron lines are not necessarily of like intensity.

The intensity of the zinc lines does not seem to vary to a significant degree in any specimen of skin. This indicates not only that zinc is unchanged in neurodermatitis but also that zinc is probably a constant constituent of the cutaneous protoplasm, although Eggleton [15] stated that it is not an essential element of nutrition.

UNAFFECTED NEURODERMATITIS SKIN

The specimens of unaffected skin studied spectrographically were taken from patients whose active lesions were also studied spectrographically, as indicated in the table.

A comparison of the minerals in a specimen (50) of unaffected skin with a specimen (33) of an active neurodermatitic lesion in the same patient reveals that whereas the unaffected skin possessed plenty of iron and calcium, these elements were lost in the active lesion. The amounts of copper and magnesium remained unchanged by the developing lesion. There was not much phosphorus in either place.

Even though the magnesium content of unaffected neurodermatitis skin is much below that of normal skin, the calcium content is in general much higher than that of normal skin. The magnesium remains essentially the same in active lesions and in unaffected neurodermatitis skin, while the calcium, and perhaps the iron content, shifts. These changes hold with but slight individual differences in the specimens of unaffected skin and of active neurodermatitic lesions in our collection.

HEALED NEURODERMATITIC LESIONS

Specimen 60 of a healed lesion, specimen 33 of an active lesion and specimen 50 of unaffected skin were from the same patient (table).

Specimen 61 of a healed lesion and specimen 29 of an active lesion were from one patient, but no unaffected skin was obtained.

The specimen (60) from a healed lesion had regained its calcium content, which was far above that present in the specimen of unaffected skin. The magnesium remained low in this case, although it was increased in amount in 2 other cases. In none of the 6 healed lesions of which we had spectrograms (although not all were read microphotometrically) was the amount of calcium reduced, the values for this element in most of these cases being much increased over normal. The magnesium is sometimes, but not always, increased in amount over that present in active lesions and unaffected skin. There is an excess amount of iron present in every healed lesion, although this may be accounted for by blood extravasations. The excess calcium in these spectrograms of healed lesions is probably not due to the presence of extravasated blood, because, as will be shown in a subsequent paper, the epidermis is heavily laden with white ash of calcium and magnesium in micro-incinerated sections.

OTHER CUTANEOUS DISEASES

None of the pathologic controls showed the same changes as were found in neurodermatitis, with the possible exception of xeroderma pigmentosum and exfoliative dermatitis. Since we had only 2 cases of the former and only 3 of the latter, the comparison with neurodermatitis is not on a sufficiently broad basis. However, the specimens from the case of xeroderma pigmentosum and from the 2 of exfoliative dermatitis, not estimated photometrically, showed even stronger magnesium lines than those of normal skin.

Infantile Dermatitis.—The magnesium lines in the specimen from our single case of this disorder were more intense than in almost any of the other specimens. The intensities of the calcium and iron lines were within normal limits. These findings are interesting because infantile dermatitis is similar to chronic disseminated neurodermatitis both clinically and histologically.

Psoriasis.—The copper content of the skin in each of the 13 cases of psoriasis was increased well above the copper content of normal skin. Although this may not be a change of physiologic significance, it is well worth noting and will be discussed later. The intensity of the magnesium lines in psoriasis is within the normal range.

Exfoliative Dermatitis.—In the 3 cases of exfoliative dermatitis it was observed that while the magnesium lines approached a normal intensity (the case reported being that with the least dense lines for magnesium), the calcium content was always slightly higher than normal. Ashed sections of this skin indicated that there was little iron present, but the epidermis was so heavily loaded with white ash of calcium and

magnesium that the cellular structure was indistinguishable. The copper and iron lines, while of low intensity, were still within normal limits.

Contact Dermatitis.—In none of our cases of contact dermatitis did the determinations differ greatly from normal. However, in the specimens of most of our 8 cases (only 4 of which were read photometrically) the magnesium lines were of much greater intensity than those of normal skin.

Chronic Dermatitis.—In the specimens from the 3 patients with chronic dermatitis, the magnesium lines were unusually heavy, while the calcium lines were very much less intense than those generally seen in normal skin.

Localized Neurodermatitis.—Spectrographic analysis of specimens from our 6 patients with localized neurodermatitis (lichen simplex chronicus Vidal) revealed that the magnesium content was well within the normal range and in some cases high, with the exception of 1 case in which the magnesium content was low and the calcium content was high. The calcium content in the skin of the other 5 patients with this disease was within normal limits. In this exceptional case, with the low magnesium value, the iron lines were more intense than in any of the other cases. This specimen was taken from a woman aged 71 whose eruption began shortly after contact with garden weeds.

ELEMENTS FOUND IN NEURODERMATITIS SKIN

Although no elements of known pathologic significance have been detected in neurodermatitis skin, it is perhaps of some value to list those found by spectrographic analysis: calcium, magnesium, phosphorus, potassium, sodium, manganese, zinc, iron, aluminum, copper, boron, silicon and strontium. These elements are ordinary constituents of almost all protoplasm and are not to be considered of unusual occurrence. With the exception of those previously discussed, no other decided differences either qualitatively or quantitatively were observed in the minerals in the active lesions of neurodermatitis, in unaffected neurodermatitis skin and in the healed lesions of this disease.

COMMENT

Magnesium is definitely decreased in amount in every active lesion and in every area of unaffected skin which we have examined from patients with chronic disseminated neurodermatitis. It is low in most of the healed lesions as well. Normal skin contains comparatively large amounts of magnesium. In none of the patients with the thirteen other cutaneous diseases studied was there a deficiency in magnesium in the skin. It appears, then, that chronic disseminated neurodermatitis is characterized by a cutaneous magnesium deficiency. The absence of

symptoms of a general magnesium deficiency in patients with disseminated neurodermatitis suggests that the magnesium deficiency may be limited to the skin. No cases of a disease characterized by a magnesium deficiency have hitherto been reported in man, although many instances of magnesium deficiency have been described in rats, cattle and other animals.

Ten years ago McCollum and Orent [22] prepared a diet which contained 0.18 mg. of magnesium per hundred grams of food. They fed this low magnesium diet to rats and demonstrated for the first time the spectacular series of symptoms which are typical of severe magnesium deficiency. It is interesting that vasodilatation and hyperemia of the skin and hyperexcitability were observed in these rats, much as they are observed in patients with neurodermatitis. However, in rats the condition terminates with convulsions and death unless the magnesium is restored to the necessary amount. In the few animals that survived the convulsions trophic changes developed in the epidermal structures and edema in the extremities. The gums of these rats became hypertrophied with fibrous tissue growths. The addition of small amounts of magnesium to the diet quickly corrected these abnormalities.

The magnesium deficiency peculiar to the skin of patients with neurodermatitis is not the result of a low magnesium diet, since the food and blood serum of patients suffering from this disease contain sufficient quantities of magnesium. The skin apparently does not retain or accept biologically essential amounts of magnesium, but whether the defect is in the skin itself or in the blood vascular system cannot as yet be determined. Experiments on rats are in progress which will enable us to study the mineral changes in other sorts of tissue as well as in the skin at various stages of the development of an induced magnesium deficiency.

In the skin of patients with neurodermatitis copper does not seem to be associated with the production of melanin, for in unaffected skin that is hyperpigmented copper does not occur in necessarily greater quantity than in active lesions in which depigmentation is complete.

Similarly, in the skin of patients with xeroderma pigmentosum in which the basal and some spinous cells are heavily pigmented, copper is not any more abundant than in depigmented specimens of skin. There is little or no pigmentation in the skin of patients with psoriasis, yet the copper content of such skin tends to be much higher than in any other case on our records.

Cunningham [14] found that the copper content of skin from black rats and rabbits tends to be higher than that from albinos and suggested that

22. McCollum, E. V., and Orent, E. R.: Effects on the Rat of Deprivation of Magnesium, J. Biol. Chem. **92**:xxx, 1931.

copper might serve as a catalyst in melanogenesis. Yoshikawa [23] noted that senile depigmentation of human hair is accompanied by a decrease in the copper content of hair. This is not due to age, according to Yoshikawa, because the copper content of black hair is constant irrespective of age. The low copper content of old hair is associated with diminished melanin production.

Although it is impossible to make any positive assertions regarding the indispensability of zinc, it is important to note that the zinc content of normal and of pathologic specimens of skin in our series of cases was fairly constant. Stirn, Elvehjem and Hart [24] reported that zinc is an essential element in nutrition, for they observed retardation of growth and interference with the development of a normal coat of hair in rats fed a low zinc diet.

Zinc does not appear to be concerned in the development of neurodermatitis, but our observations indicate that it is a constant constituent of cutaneous protoplasm. Eggleton [15] observed that the zinc content of epidermal structures varies so much that he stated the belief that this substance is merely an inactive storage element being eliminated by way of the integument.

SUMMARY AND CONCLUSIONS

Thirty-three biopsy specimens of skin from patients suffering with chronic disseminated neurodermatitis were analyzed spectrographically and compared with 83 biopsy specimens of normal human skin and with 55 specimens from patients with thirteen other cutaneous diseases.

The magnesium content of the skin of patients with chronic disseminated neurodermatitis is decidedly reduced in unaffected neurodermatitis skin from the region of the midaxillary line in active lesions and in healed lesions.

It is believed that chronic disseminated neurodermatitis is characterized by a magnesium deficiency in the skin, for no reduction of this element is apparent in any other cutaneous disease studied.

Analysis of the skin in 6 cases of localized neurodermatitis (lichen simplex chronicus Vidal) revealed that it contained normal amounts of magnesium (with the exception of 1 case in which the diagnosis was questionable).

Zinc is a constant constituent of cutaneous protoplasm.

No evidence of a relation between copper and pigmentation is found in the skin of patients with neurodermatitis.

The elements found spectrographically in neurodermatitis skin are as follows: calcium, magnesium, potassium, sodium, phosphorus, aluminum, manganese, zinc, iron, copper, boron, silicon and strontium.

23. Yoshikawa, H.: Biochemistry of Copper: XX. Copper in Keratinous Appendages of the Skin, Jap. J. M. Sc., II, Biochem. **3**:269, 1937.

24. Stirn, F. E.; Elvehjem, C. A., and Hart, E. B.: The Indispensability of Zinc in the Nutrition of the Rat, J. Biol. Chem. **109**:347, 1935.

PREVENTION OF TRANSFUSION SYPHILIS

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In an article read at a meeting of the Section on Dermatology of the Medical Society of the State of Pennsylvania in October 1938,[1] a complete summary of cases of syphilis acquired by transfusion showed that of 41 cases reported, in 16 examination of the donor's blood for syphilis would not have detected its presence (table 1). In 6 donors the condition was in the incubation period of the chancre; in 9 there were chancres which were not discovered and Wassermann reactions were negative.

One donor was under active treatment for syphilis and had a negative Wassermann reaction just before the transfusion, but shortly after that active malignant syphilis developed while treatment was being given. In 2 other cases the emergency was too great to allow time for performance of blood tests. In 39 per cent of the recorded cases, therefore, examination of the donor's blood before transfusion would not have protected the recipient.

Our animal experiments, made before the publication of the aforementioned article, were inconclusive, as none of our control rabbits acquired syphilis. During these experiments the temperature in the animal house was raised to over 100 F. for some hours through mechanical failure of the plant, and this high temperature probably prevented the infection.

Feeling that checking the donor for syphilis by testing the blood before transfusion is an inadequate method of protecting the recipient, we decided to try prevention by adding a spirocheticidal drug to the blood before transfusion. Previous efforts to do this with mercurials were unsuccessful, as shown in our previous reports.

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Read at the Sixty-Fourth Annual Meeting of the American Dermatological Association, Inc., New Orleans, April 8, 1941.

1. Eichenlaub, F. J., and Stolar, R.: Syphilis Acquired from Transfusion, and Its Control, Pennsylvania M. J. **42**:12, 1939.

We selected mapharsen as the best drug for this purpose for the following reasons: (1) it is a direct spirocheticide and does not require chemical reaction to form the active arsenoxide; (2) it has a low toxicity, and (3) the amount of arsenic is so small that it seems improbable that it would affect even a patient who was extremely ill, the arsenic content being 27 to 29 per cent, or approximately 0.003 Gm. per 0.01 Gm. of mapharsen.

According to Gruhzit, Lindsay, Hendricks and Dodd [2] the sterilizing dose of mapharsen for rabbits is 2 mg. per kilogram of body weight. For the usual 500 cc. transfusion, therefore, 1 mg. of mapharsen should kill all spirochetes present in the blood. Feeling that a dose of 0.01 Gm. per 500 cc. of blood would prove harmless and, as it is ten times the effective sterilizing dose, should be protective, we have done our work with this amount as a basis.

TABLE 1.—*Stage of Syphilis in Donors**

Primary (Incubation Period)	Primary (Wassermann Reaction Negative)	Primary (Wassermann Reaction Positive)	Secondary	Latent	Emergency (No Investigation of Donor)
6	9	3	4	16	2

* One donor was under active treatment and had a negative Wassermann reaction just before giving the transfusion.

EXPERIMENTS

A suspension of Spirochaeta pallida, Nichols-Hough strain, was prepared by macerating a testicular chancre of a rabbit and adding physiologic solution of sodium chloride. The filtrate contained 20 to 30 actively motile spirochetes per oil immersion field. Two cubic centimeters of this suspension was added to 18 cc. of whole citrated blood and a similar amount to 18 cc. of clear blood serum. The two preparations were then divided into two separate samples of 10 cc. each. In 10 cc. of the whole citrated blood and in 10 cc. of the serum we then placed the amount of mapharsen to make the concentration equivalent to 0.01 Gm. to 500 cc., that is, .0002 Gm.

No motile spirochetes were demonstrated by dark field examination of the serum suspension containing mapharsen at the end of fifteen minutes. No examination of the whole blood suspension was made.

Two cubic centimeters of each of these preparations was injected into the testicle of each of 19 rabbits, which were divided into the following groups: two control groups of 5 each, 5 rabbits receiving whole blood with mapharsen and 4 receiving serum with mapharsen.

2. Gruhzit, O. M.; Lindsay, W. D.; Hendricks, G., and Dodd, M. C.: Mapharsen ("Arsenoxide") in the Therapy of Experimental Syphilis and Trypanosomiasis, Arch. Dermat. & Syph. **32**:848 (Dec.) 1935.

RESULTS

In this experiment it will be seen that none of the rabbits which received blood or serum containing mapharsen were infected. Of the 5 inoculated with whole blood and spirochete emulsion without mapharsen, a testicular chancre developed in 1. Of the 4 inoculated with serum and spirochete emulsion, testicular chancres developed in 3. It appears, therefore, that in the quantity recommended the mapharsen will sterilize blood known to contain large numbers of spirochetes.

TABLE 2.—*The Prevention of Transfusion Syphilis in Rabbits by the Addition of Mapharsen to the Whole Blood or Serum Injected*

Suspension Injected (Jan. 21, 1939)	Rabbit	Results
Whole blood with mapharsen	1, 2, 3, 4, 5	No infection; all alive June 6
Whole blood without mapharsen	6	No infection; alive June 6
	7	No infection; died June 1
	8	Testicular chancre; dark field examination showed spirochetes, April 10
	9	No infection; died February 28
	10	No infection; died February 15
Serum without mapharsen	11	Injection made in back (female); no infection; alive June 6
	12	Testicular chancre; dark field examination showed spirochetes February 25
	13	Testicular chancre; dark field examination showed spirochetes March 18
	14	Testicular chancre; dark field examination showed spirochetes March 25
Serum with mapharsen	15, 16, 17, 18	No infection; alive June 6
	19	No infection; died nine weeks after injection

COMMENT

Kast, Peterson and Kolmer [3] have published the results of a similar series of experiments, in which arsphenamine and neoarsphenamine were used as the protective drugs. Their article was received for publication on Oct. 2, 1938 and therefore takes precedence over ours. A partial summary of their work is as follows:

Neoarsphenamine produced total or marked loss of motility in dilutions as high as 1:20,480 in saline solution and 1:5,120 in serum in 15 minutes and in dilutions

3. Kast, C. C.; Peterson, C. W., and Kolmer, J. A.: The Treponemicidal Activity of Arsphenamine and Neoarsphenamine in Vitro with Special Reference to Citrated Blood and a Suggested Method for the Prevention of Transfusion Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **23**:150, 1939.

as high as 1 : 163,840 in both saline solution and serum after exposure of 30 to 60 minutes at room temperature.

Final dilutions of the arsphenamine (disodium) as high as 1 : 20,480 in citrated blood were completely treponemicidal in rabbit inoculation tests (testicular) and neoarsphenamine in dilutions as high as 1 : 40,960 after an exposure of 15 minutes at room temperature.

By intravenous inoculation of rabbits, arsphenamine (disodium) was found completely treponemicidal in dilutions as high as 1 : 40,960 and neoarsphenamine as high as 1 : 20,480 (higher dilutions not being tested) after an exposure of 15 minutes at room temperature.

For the practical application of their work these authors recommended the use of 0.01 Gm. of neoarsphenamine to each hundred cubic centimeters of citrated blood. The arsenic content of neoarsphenamine is about 20 per cent, so that for a 500 cc. transfusion this would mean administering a dose of 0.01 Gm. of arsenic. In most instances this would probably prove harmless, but with certain conditions, for instance, hemorrhagic purpura and exfoliative dermatitis from arsenic, this amount might be undesirable.

CLINICAL USE

We suggest that in practice 0.01 Gm. of mapharsen be added to the sodium citrate solution when the blood is withdrawn from the donor. Dr. V. Dardinski has used this method in seven transfusions given to 5 patients at the Georgetown University Hospital. All the patients did well, and none showed any reaction from the mapharsen. One patient who received two transfusions had a generalized and severe exfoliative dermatitis, not of arsenical origin. His condition was much improved after the transfusions.

SUMMARY

Our work and that of Kast, Peterson and Kolmer seem convincing evidence that the addition of a small amount of one of the antisyphilitic arsenicals will sterilize blood known to contain large numbers of spirochetes.

A review of the reported cases of transfusion syphilis shows that the performance of a Wassermann test or one of its modifications on the donor prior to transfusion is not sufficient protection for the recipient.

As a result of our experiments we believe that the addition of 0.01 Gm. of mapharsen to the sodium citrate solution for each 500 cc. of blood will prevent the infection of recipients even though the donor has syphilis. We believe, therefore, that this measure may replace the routine checking of donors by Wassermann tests. If this method is not used routinely, it should always be used when time to investigate the donor for syphilis is too short or when any doubt as to the donor's freedom from syphilis exists.

ABSTRACT OF DISCUSSION

DR. JOHN ANTHONY GAMMEL, Cleveland: I think this paper is much more important than it might appear on the surface.

The authors mentioned that there are only 42 cases of transfusion syphilis reported in the medical literature, but I am sure, judging from my own experience, that if a poll were to be taken now it would be found that probably between 200 and 300 cases have come to the attention of the members present but have not been reported in the literature. Naturally, hospitals are not anxious to have such reports published. There is always the possibility of medicolegal complications. If the experimental work reported is applicable to the human being, it will soon be possible to advise surgical departments what to do in emergency transfusions. This work is probably also important for physicians who may have to go overseas or who work among Negroes and in places where the incidence of syphilis is high and where it may be practically impossible to obtain a donor without a positive Wassermann reaction.

DR. OTTO H. FOERSTER, Milwaukee: I have been greatly interested in this presentation and think the in vitro treatment of blood with mapharsen for transfusion purposes, as proposed, is a procedure that not only is of practical interest in civilian life but, as Dr. Gammel just stated, is one that presents possibilities of value for military medicine.

Just recently the efficiency of mapharsen in vitro as a treponemicide was demonstrated by Dr. Harry Eagle and his co-workers (*J. Pharmacol. & Exper. Therap.* **69**:342 [Aug.] 1940; **70**:211 and 221 [Oct.] 1940). This investigation was part of a comparative assay of numerous substituted phenylarsenoxides, and the report included, also, data on the toxicity and potential therapeutic utility of the substances. The authors used suspensions of pathogenic spirochetes (Spirochaeta pallida) obtained from testicular chancres of rabbits and found that immobilization, loss of infectivity and death of the organism were produced in vitro by the arsenoxides, although, it was concluded, none of the many derivatives studied, including twenty new compounds, seemed to be as potentially valuable as mapharsen in the treatment of syphilis.

The amount of chemical proposed by Drs. Eichenlaub, Stolar and Wode—10 mg. per 500 cc. of blood—can hardly be conceived, it seems to me, as presenting an element of danger other than that offered by the remote possibility of an extreme sensitivity in rare instances. Although this is perhaps more a theoretic than a practical consideration, it should not be overlooked.

The transmission of syphilis by blood transfusion is such a tragic occurrence that, even though it fortunately is rare, the procedure should be safeguarded as completely as it can be by utilizing all the scientific information available. The proposal set forth in this paper appeals to me as one that provides a reasonable and practical method for prevention. However, because of the comparative rarity of transmission, it will require a long time to obtain data that could be considered as significant.

DR. FRANK C. EICHENLAUB, Washington, D. C.: Regarding the number of cases reported, in the original article that we published we called attention to the fact that transfusion syphilis is probably at least ten times as common as the literature would lead one to believe and also to the fact that prevention of the condition is important, even though the occurrence is rare, because of the medicolegal possibilities.

Regarding the use of our proposed treatment in military medicine, about three months ago I received a letter from a London hospital asking for information about this method. Evidently something like this is being sought in England.

CHRYSIASIS

OTTO E. L. SCHMIDT, M.D.
CLEVELAND

DEFINITION AND HISTORY

Chrysiasis (synonyms for which are auriasis, chrysoderma and *hautaurosis*) is a permanent pigmentation of the skin caused by the parenteral use of a gold preparation and the subsequent exposure of the skin to ultraviolet radiation, including sunlight.

Gold preparations given intravenously began to be used extensively in the treatment of pulmonary tuberculosis in 1917 (krysolgan), and Möllgaard [1] introduced gold sodium thiosulfate (under the name sanocrysin) in 1924. Nine years later Fellner [2] listed and described sixteen gold preparations tried in nearly all branches of dermatosyphilology.

Early in its use gold was found to cause numerous mild to severe side actions,[3] but not until 1928 did Hansborg [4] describe the first observed case of chrysiasis, as follows:

> A 20 year old white woman with auburn hair and light complexion exhibited a slate gray pigmentation on the exposed parts (face, neck and hands). The color of the skin resembled that seen in argyria. The patient had been treated two years previously for pulmonary tuberculosis with twenty-six injections of sanocrysin (12.35 Gm., = 4.62 Gm. of elemental gold). There had been no reactions at the time of treatment.

From the Department of Dermatology and Syphilology of Western Reserve University School of Medicine and of the University Hospitals.

A preliminary report of an investigation being conducted under a grant from the Committee on Therapeutic Research of the American Medical Association.

1. Möllgaard, H.: Chemotherapy of Tuberculosis, Copenhagen, Nyt Nordsk Forlag, 1924.

2. Fellner, M.: Die Goldtherapie in der Dermato-Venerologie, Zentralbl. f. Haut- u. Geschlechtskr. **43**:489 and 585, 1933.

3. (*a*) Anderson, N. L., and Palmer, W. L.: The Danger of Gold Salt Therapy: Report of Fatal Case, J. A. M. A. **115**:1627 (Nov. 9) 1940. (*b*) Copeman, W. S. C., and Tegner, W.: A Review of Gold Therapy, Lancet **1**:554, 1937. (*c*) Driver, J. R., and Weller, J. N.: Untoward Results from the Use of Gold Compounds: Report of Fatal Case, Arch. Dermat. & Syph. **23**:87 (Jan.) 1931. (*d*) Fellner.[2] (*e*) Mayer, R. L.: Chrysiasis; Auriasis, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 4, pt. 2, p. 85.

4. Hansborg, H.: Chrysiasis-Ablagerung von Gold in Vivo, Acta tuberc. Scandinav. **4**:124, 1928.

The second and third cases of gold pigmentation of the skin were American cases and were reported by Schamberg [5] in 1928 and by Zimmerli and Lutz [6] in 1929. Thereafter occasional instances were described,[7] mainly from Scandinavia, and it was not until 1938 that Kochs [8] described, as follows, the first German case:

A white woman 56 years of age had been treated for chronic discoid lupus erythematosus over a twelve year period with courses of various gold preparations (equivalent of 22.57 Gm. of elemental gold). In November 1937 a bluish gray pigmentation was noted in parts which had been exposed to light, i. e., the face, neck and hands. The lupus scars were deeply pigmented.

Although no accurate statistics are available, it is evident from a review of the literature that chrysiasis is a rarely recognized side action of gold therapy; that it may be more common than is supposed, however, will be indicated in another section of the paper.

DESCRIPTION AND MODE OF APPEARANCE OF CHRYSIASIS

In all cases except one chrysiasis followed the intravenous injection of gold, either in a colloidal form or in chemical combination. In Schamberg's [5] case there was local pigmentation, which he designated as "chrysoderma," within a few days after the accidental subcutaneous injection of a colloidal gold preparation.

In the reported cases the majority of patients had pulmonary tuberculosis and were receiving no other heavy metal therapy. Other conditions during the treatment of which chrysiasis occurred were psoriasis and lupus erythematosus; in both of these the pigmentation appeared most intensely in the lesions of the disease being treated.

The color of the affected skin has been variously described as a uniform barely perceptible gray, slate gray, grayish purple ("livid"),

5. Schamberg, J. F.: Chrysoderma: A Permanent Gold Staining of the Skin, Arch. Dermat. & Syph. **18**:862 (Dec.) 1928.

6. Zimmerli, E., and Lutz, W.: Eine eigenartige Form von Pigmentierung nach Goldbehandlung, Arch. f. Dermat. u. Syph. **157**:523, 1929.

7. (*a*) Jäger, B.; Kohl, F., and Brunotte, H.: Grundsätzliche Erwägungen in Anschluss an einen Fall von Golddermatitis (Triphal), Arch. f. Dermat. u. Syph. **154**:76, 1928. (*b*) López, P.: Aurosis cutánea en el curso del tratamiento por la sanocrisina, Progresos de la clin. **39**:402, 1931; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **39**:75, 1932. (*c*) Lorenzen, J. N.: Ueber das Auftreten von Chrysiasis bei früher mit Natriumaurothiosulfat behandelten Lungentuberkulösen, Beitr. z. Klin. d. Tuberk. **76**:686, 1930. (*d*) Sallmann, L.: Ueber Augenveränderung bei menschlicher Chrysosis nach Sanocrysinbehandlung, Ztschr. f. Augenh. **79**:208, 1932; cited by Mayer.[3e] (*e*) Fowler, W. C.: A Note on the Occurrence of Chrysiasis Following Treatment by Gold Salts, Tubercle **16**:539, 1935.

8. Kochs, A. G.: Zur Kenntnis der Chrysiasis, Arch. f. Dermat. u. Syph. **178**:323, 1938.

grayish blue, bluish violet, blue-green and brownish yellow. A reticular type of pigmentation has also been described.[3e] Cascos [9] reported a salmon red coloration of the oral mucosa in a case of chrysiasis.

The distribution of the coloring is on the exposed portions of the body: face, eyelids,[10] scleras,[7d] neck (and the upper part of the chest, the V portion, in women), arms and hands. The relation between the appearance of chrysiasis and exposure to sunlight was recognized from the first [11] and has been demonstrated clinically by the absence of coloration deep in the natural folds and creases of the skin in areas which show frank pigmentation.[12] Kochs [8] was able to produce typical gold pigmentation in the unpigmented skin of the back of a patient suffering from chrysiasis of the exposed portions of her skin by exposure to an erythema dose of ultraviolet radiation. Another of Kochs's patients, who had received large doses of a gold preparation (total equivalent of 5.75 Gm. of the element) over an eight and one-half year period, had no frank chrysiasis, but his skin was strongly positive for gold on spectroscopic examination of a biopsy specimen. This author thus introduces the concept of "latent" chrysiasis.

INCIDENCE AND INDIVIDUAL FACTORS

Chrysiasis has thus far been observed only in the white race and mostly in persons of northern European extraction. Hansborg expressed the opinion that a blond complexion, naturally relatively pigment free, predisposed to the development of gold pigmentation. In a study of 57 patients who received varying amounts of gold sodium thiosulfate, Lorenzen [7c] was unable to find any correlation between the natural pigmentation of the skin, hair and eyes and the development or severity of chrysiasis in 28 of these.

The ages of reported patients with chrysiasis varied from 17 years to 67, with an average of 33. By far the larger proportion of patients with gold pigmentation have been women (in 23 of 34 cases in which identifying data were given); probably a large factor in this sex distribution is based on cosmetic considerations (i. e., the greater likelihood of women to note and report variations from the normal color of their skin to their physicians).

Attention was drawn to the possible predisposing effect of an antecedent acute reaction to gold therapy (e. g., eczematous dermatitis or acute erythema) by Zimmerli and Lutz. In their case of chrysiasis an

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9. Cascos, A.: Etude comparative des pigmentations métalliques. Argyrose et chrysose, Ann. de dermat. et syph. **7**:751, 1936.

10. Fowler.[7e] Sallmann.[7d]

11. Hansborg.[4] Zimmerli and Lutz.[6] Lorenzen.[7c] Fowler.[7e]

12. Zimmerli and Lutz.[6] Salimann.[7d] Kochs.[8]

erythematous dermatitis had developed on the extremities one and one-half years before the onset of gold pigmentation of the exposed parts. Preceding dermatitis was mentioned in the reports of 2 other cases.[13]

Extremely important is the influence of dosage on the appearance and severity of chrysiasis. This was well shown by Lorenzen, who studied 57 patients who were available in a group of 143 treated during the period from 1923 to 1930 with gold sodium thiosulfate for pulmonary tuberculosis. Of this number, 28 (49 per cent of those studied) had definite chrysiasis. Correlating pigmentation with dosage, the author concluded that (*a*) no patient who received a total dose of less than 50 mg. of gold sodium thiosulfate per kilogram of body weight had definite chrysiasis and that (*b*) no patient who received a total dose of 150 mg. of gold sodium thiosulfate per kilogram of body weight escaped the development of chrysiasis.

Kochs also considered gold pigmentation undoubtedly to be due to overdosage. Egües [14] reported 10 cases of chrysiasis in a group of 90 patients (11 per cent) treated with gold sodium thiosulfate. Those afflicted received total doses of 14 to 24 Gm. of the drug. If one assumes the weight of an average man to be roughly 60 Kg., this dose in milligrams per kilogram of body weight would be 233 to 400 mg.

The time interval between the administration of the gold compound and the onset of clinical chrysiasis shows considerable variation; some investigators [15] have observed the specific pigmentation develop during the period of treatment with gold. In most cases, however, a variable latent period of one month to five years elapses before chrysiasis makes its appearance. In the largest group studied by one author [7e] the phenomenon was observed at the end of the first year and during the course of the second year following gold therapy.

DIFFERENTIAL DIAGNOSIS

Chrysiasis is to be distinguished from argyria by the history of the use of the suspected heavy metal, by the presence of the characteristic pigmentation on the exposed parts only (gold) or on the covered parts also (silver) and by the histologic and chemical examinations. Hemachromatosis may be differentiated by the typical brown pigmentation, associated diabetes and hepatomegaly and by the demonstration of iron pigment histochemically.

Riehl's melanosis, Addison's disease, ochronosis, tanning (by sunlight), chloasma and vagabond pigmentation must also be differentiated.

13. Jäger, Kohl and Brunotte.[7a] Fowler.[7e]

14. Egües, J.: Observaciones de crisiasis, Rev. Asoc. méd. argent., cited by Fowler.[7e]

15. Zimmerli and Lutz.[6] Fowler.[7e] Kochs.[8]

DISTRIBUTION OF GOLD IN VIVO

The fate of gold in the body of man and experimental animals has been thoroughly studied.[16] After intravenous injection it is eliminated slowly from the body, Hansborg finding considerable quantities in the urine and feces two years after cessation of therapy and Kochs finding strong traces in the sweat as well. Christeller, Kochs and others found large traces in the circulating blood, largely in the plasma.

All observers agree that gold is mainly taken up by the reticuloendothelial system and the free tissue histiocytes. Kurosu [17] stated that after subcutaneous injection: "The fact that a large quantity of gold is found with regularity in this place (i. e., the site of subcutaneous injection) shows that gold sodium thiosulfate is rapidly disintegrated before it can enter the circulation and that it (the gold) is taken up by the massive accumulation of phagocytes at the site of injection . . . As our experiments on healthy mice have shown, with small doses the site of injection may be the only place of gold deposition."

In mice, guinea pigs, rabbits, dogs [18] and man the largest concentration of gold is found usually in the kidney (in or near damaged renal tubules) or in the liver (in the Kupffer cells); other depots are the spleen, large intestine, lung, lymph nodes and skin. It is not present in the hair, nails, stratum corneum of the epidermis or the parenchyma of the central nervous system.

In an exhaustive experimental study of the distribution of gold in both normal and tuberculous rabbits, appreciable quantities of gold were found in the raw hide (*Pelz*) of each animal.[19] With the use of gold sodium thiosulfate (37.35 per cent elemental gold) and sodium auroallylthiourea benzoate (lopion) (42 per cent elemental gold) in total doses ranging from 0.29 to 2.33 Gm., the quantities of gold in the hide varied from 2.3 to 25.7 mg. per hundred grams, averaging 8.7 mg., of elemental

16. (*a*) Brahn, B., and Weiler, G.: Die quantitative Verteilung des Goldes in den Organen gesunder und tuberkulöser Kaninchen nach Behandlung mit Goldpräparaten, Biochem. Ztschr. **197**:342, 1928. (*b*) Christeller, E.: Ein microchemischer Goldnachweis im Gewebe, Verhandl. d. deutsch. path. Gesellsch. **22**:173, 1927. (*c*) Henins, K., and Weiler, G.: Die quantitative Verteilung des Goldes in den Organen gesunder und tuberkulöser Kaninchen nach Behandlung mit Goldpräparaten: Teil II, Biochem. Ztschr. **214**:204, 1929. (*d*) Fellner.[2] Mayer.[3e] Kochs.[8]

17. Kurosu, S.: Ein histochemischer Goldnachweis, zugleich ein Beitrag zur Frage der Verteilung und Ausscheidung des Sanocrysins im gesunden und tuberkulösen Körper, Ztschr. f. d. ges. exper. Med. **57**:77, 1927.

18. Borchardt, H.: Ueber die experimentelle Chrysosis bei Kaninchen und Hunden und ihren histochemischen Nachweis, Virchows Arch. f. path. Anat. **267**:272, 1928.

19. Brahn and Weiler.[16a] Henins and Weiler.[16c]

gold. There was no direct relation between size of dose and concentration in the skin, although, roughly, the larger the dose, the higher the concentration.

Schamberg injected two colloidal gold preparations subcutaneously into 2 rabbits; almost immediately a permanent indigo stain of the skin surrounding the injection site developed. A similar injection of gold sodium thiosulfate in one rabbit produced no perceptible change in three months.

HISTOLOGIC PICTURE

The microscopic appearance of gold pigmentation of the skin has been well described by Zimmerli and Lutz, Wigley,[20] Kochs and others:

Epidermis.—Here the architecture is unchanged. No granules of gold are present in any of the layers except possibly the stratum mucosum in 1 case.[5]

Cutis.—The principal pathologic changes are found in the pars papillaris and the upper part of the pars reticularis. Here, staining with hematoxylin and eosin, after ordinary fixation in a solution of formaldehyde and clearing, shows a deposit of abnormal pigment. This consists of small, irregularly sized round or oval deep black granules, mostly agglomerated in endothelial and adjacent wall cells of the blood and lymph vessels and in free histiocytic cells. Occasional granules apparently lie free in the tissue spaces and rarely are arranged in line as though plastered to elastic fibers. The blood vessels may appear slightly dilated, but there was only 1 instance of perivascular infiltrate in the pars papillaris; no other evidence of inflammatory changes has been reported.

To identify the nature of the granules, microchemical incineration methods[21] readily demonstrate the presence of gold in the tissues. Christeller,[16b] Kurosu[17] and Henriques and Okkels[22] have devised and used a microchemical method for revealing the presence of gold in the skin and in other tissues based on the familiar Cassius purple reaction. Christeller noted that this may be verified (after treatment with acid and alkali to dissolve confusing deposits) by the solubility of the gold granules in potassium cyanide solution.

Study of the unstained fixed sections by means of the dark field illuminator[5] has proved valuable. Cascos,[9] using a modification of

20. Wigley, J. E. M.: Some Observations on the Deposition of Gold in the Skin, Brit. J. Dermat. **44**:69, 1932.

21. Borchardt.[18] Wigley.[20] Brahn and Weiler.[16a] Henins and Weiler.[16c]

22. Henriques, V., and Okkels, H.: Histochemische Untersuchungen über die Ablagerungweise von Gold und Blei innerhalb des Organismus, Arch. f. d. ges. Physiol. **225**:364, 1930.

E. Hoffmann's [23] "Leuchtbildmethode," made the following distinction between gold and silver pigmentation of the skin by dark field examination:

CHRYSIASIS	ARGYRIA
Large granules of unequal size.	Small uniformly sized granules.
Deposition in macrophages and in walls of dermal blood vessels (reticuloendothelial system).	Pigment in hair follicles, capsules of sebaceous or sudoriferous glands, arrector pili muscles or diffuse subepidermal areas.

Gerlach [24] and Kochs demonstrated the nature of the gold pigmentation by spectrographic methods.

TREATMENT OF CHRYSIASIS

As in argyria, no treatment has successfully been devised for chrysiasis. Fowler [7e] expressed the opinion that in his case there was a fluctuation in the intensity of the pigmentation depending on the amount of exposure to sunlight. Prophylaxis has been stressed by all observers of this side action of gold therapy as the principal method whereby chrysiasis may be combated. This consists essentially of three main precautions: (1) keeping the total doses of gold preparations well below the limits indicated by Lorenzen, namely, 50 mg. of gold sodium thiosulfate per kilogram of body weight; (2) avoiding undue exposure to sunlight or other sources of ultraviolet radiation, and (3) care in averting paravenous infiltrations while the drug is being administered.

SUMMARY AND CONCLUSIONS

Pigmentation of the skin, chrysiasis, is not uncommon after excessive gold therapy.

The color varies from a light gray to a bluish violet or brownish yellow. There is a definite relation between exposure to sunlight and pigmentation.

Lorenzen observed that no patient receiving a total dose of less than 50 mg. of gold sodium thiosulfate per kilogram of body weight had definite chrysiasis and that no patient escaped having the condition if the total dose received was 150 mg. per kilogram of body weight.

Gold salts after injection are eliminated slowly from the body.

The only treatment of chrysiasis is prophylaxis; the dose must be kept within safe limits, i. e., under 50 mg. of gold sodium thiosulfate per kilogram of body weight.

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23. Hoffmann, E.: Die Bedeutung der Leuchtbildmethode zur Darstellung von Mikroorganismen, Dermat. Ztschr. **33**:1, 1921.

24. Gerlach, Walther, and Gerlach, Werner: Der Elementnachweis im Gewebe: II. Der Gold- und Silbernachweis im Gewebe, Virchows Arch. f. path. Anat. **282**:209, 1931.

PIGMENT PRODUCTION BY FUNGI

I. NUTRITIVE REQUIREMENTS

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In the routine identification of fungi, minute structural changes such as the size and arrangement of spores are seldom important. Undue emphasis on points of microscopic differentiation might even be misleading, as for instance in certain fluffy colonies suspected of being Trichophyton gypseum or Trichophyton purpureum, for with both organisms the fuseaux are infrequent, spiral forms are uncertain but may be present and microconidia and mycelium are similar. In other words, the microscopic picture is not definitive. The gross cultural appearance by itself is not always significant unless one includes the pigment produced in the substrate. This production of pigment is not generally appreciated as a constant characteristic of certain fungi. Our observations indicate uniform pigment formation with both T. purpureum and Microsporum lanosum. With T. purpureum a rose purple pigment is typical, and we have never observed a similar hue in the environment of any other species of pathogenic fungus. With M. lanosum a canary yellow pigment is similarly developed and is constant for this species. Maximum color and minimal filamentous growth occur when implants are made on corn meal agar. Because of the individual characteristics of the strain, the color may or may not be visible from the surface on ordinary isolation mediums but may always be observed from the under side of the colony.

The medium which we now use differs from Weidman's Pennsylvania medium [1] in that we employ Difco peptone, which was found to be interchangeable with Fairchild's peptone. The complete formula is as follows: crude American dextrose 40 Gm., Difco peptone 10 Gm., Difco granular agar 18 Gm. and distilled water 1,000 cc. The *p*H is from 5.6 to 6.

Aided by a grant from the John and Mary R. Markle Foundation.

Read at the Sixty-Fourth Annual Meeting of the American Dermatological Association, Inc., New Orleans, April 9, 1941.

From the New York Hospital and from the Department of Medicine (Dermatology), Cornell University Medical College.

1. Weidman, F. D., and Spring, D.: Comparison of Ringworm Culture Ingredients: II and III, Arch. Dermat. & Syph. **18**:829 (Dec.) 1928.

Pigment production should be clearly differentiated from the inherent color of certain fungi. The aerial growth of T. purpureum is white, whereas the similar growth of Hormodendrum pedrosoi is black. The mycelium and spores of T. purpureum are colorless when examined, while the mycelium of H. pedrosoi is black, indicating that the color is due to an inherent factor of that fungus.

It is well known that after repeated subcultures of occasional strains of some fungi, such as T. purpureum, pigment may fail to develop in the substrate. We do not know why this occurs but feel that it is limited to a few strains which have been transferred many times. Aging

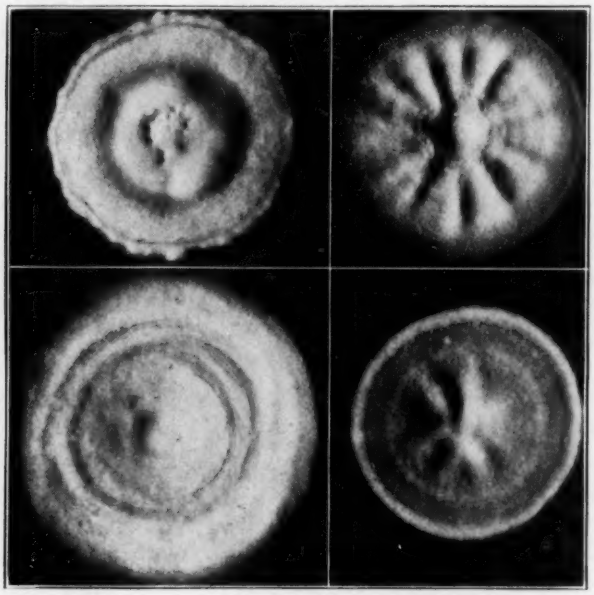

Fig. 1.—Four strains of T. purpureum on dextrose isolation medium demonstrating gross cultural differences. The development of rose purple pigment was constant.

in itself does not seem to reduce the production of pigment, but from observations of M. lanosum there would seem to be a coincidental lessening of pigment formation with the appearance of pleomorphic growth. We have not encountered any strain of T. purpureum in which pigment did not appear in the substrate on the primary isolation medium and with repeated subcultures; the original color has been maintained for over three years. In a strain of T. purpureum in which a sector developed, the rose purple pigment was heavily present under the sector, but sparse in the remainder of the colony. Samples of the two portions of the colony were seeded, and the colony which developed from the sector produced heavy pigment in the substrate, whereas no pigment

was found in the colony which developed from the other specimen (fig. 2). Since T. purpureum occasionally forms sectors, this may be one of the reasons for the loss of power to produce pigment.

Pigment appearing adjacent to a fungous growth would seem to be dependent to some degree on exogenous factors. A likely factor appeared to be the composition of the culture medium.

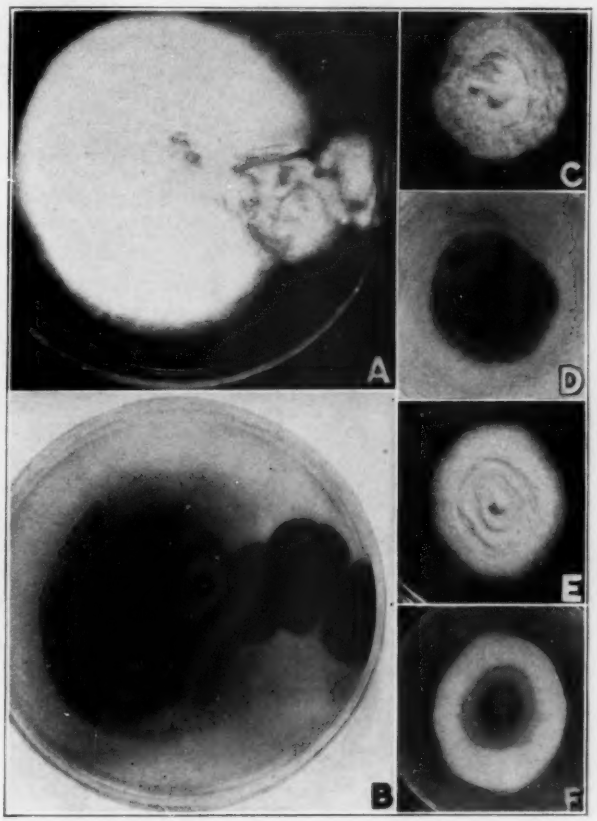

Fig. 2.—*A*, development of a sector in a colony of T. purpureum. *B*, view from the under side of the colony revealing rose purple pigment under the sector and to a lesser degree under the remainder of the colony. *C*, seeding from the sector resulted in the development of a typical growth, in which pigment may be seen from the surface. *D*, view of the colony shown in *C* from below shows pigment in the medium under the entire colony. *E* and *F*, seeding from remainder of the colony shown in *A* resulted in a colony in which no rose purple pigment developed in the substrate.

EXPERIMENTAL STUDIES

In the following experiments to attempt to determine the nutritive requirements for the formation of pigment, T. purpureum and M.

lanosum were used. The brown pigment of T. gypseum was also shown to appear when this micro-organism was grown under similar conditions.

1. Of the three active ingredients in our isolation medium, agar was eliminated from consideration by the use of a fluid medium. The absence of agar did not prevent the formation of pigment.

2. Peptone was also found to be not essential, since pigment will develop in mediums, such as carrot decoction agar, in which peptone is absent. Asparagine was found to be a satisfactory substitute for peptone.

3. Three commercial preparations of peptone were compared. These were Fairchilds, Difco and Chassaing. No appreciable difference in the degree of intensity of pigment formation was noticed (fig. 3).

4. The development of pigment seemed to depend on the sugar component. Both Sabouraud's original formula [2] and the formula for

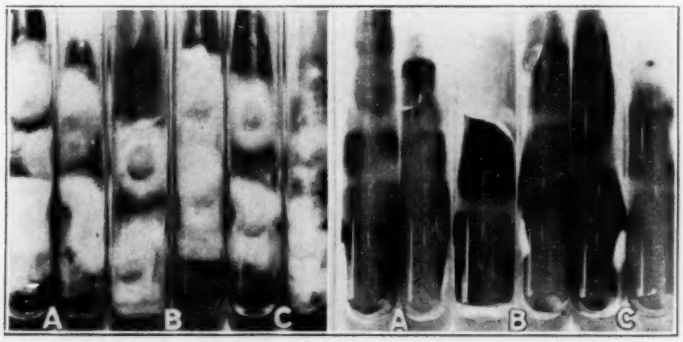

Fig. 3.—The development of pigment as well as of comparable cultural features was unaffected by changes of peptone when a crude sugar was used. *A*, Chassaing peptone. *B*, Fairchild peptone. *C*, Difco peptone.

Weidman's proof agar [1] specified a crude sugar. We wondered if the necessary component was a sugar or an impurity. For this reason we used crude dextrose, crude maltose, pure dextrose and pure maltose, each in a separate medium, and compared the results of seeding. Pigment appeared and was similar no matter whether crude dextrose, crude maltose or pure dextrose was used; in the pure maltose agar no pigment developed (fig. 4). Since pigment was present in the medium containing pure dextrose, it was apparent that impure ingredients were not necessary. Crude maltose contains dextrose and levulose as impurities, and it seemed possible that the pigment which formed when crude maltose was used was due to one of these sugars, since with pure maltose pigment did not develop.

2. Sabouraud, R.: Milieux de culture des champignons (Technique de fabrication des géloses sucrées dites: Milieux d'épreuve), Ann. de dermat. et syph. **9**:99, 1908.

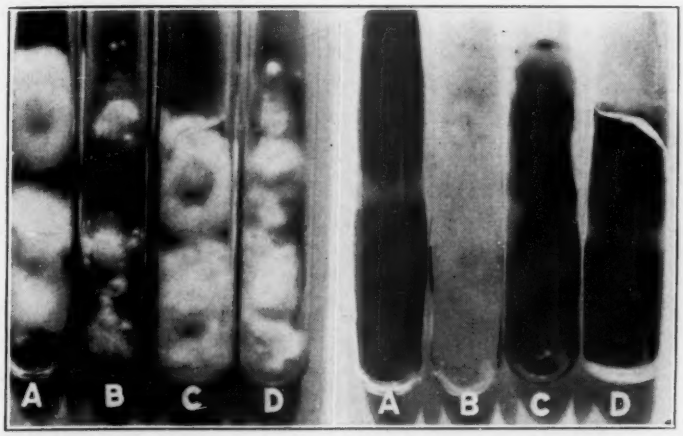

Fig. 4.—Colony of T. purpureum seeded on mediums containing: (*A*) crude maltose, (*B*) pure maltose, (*C*) crude dextrose and (*D*) pure dextrose. Pigment developed satisfactorily in all but the medium containing pure maltose.

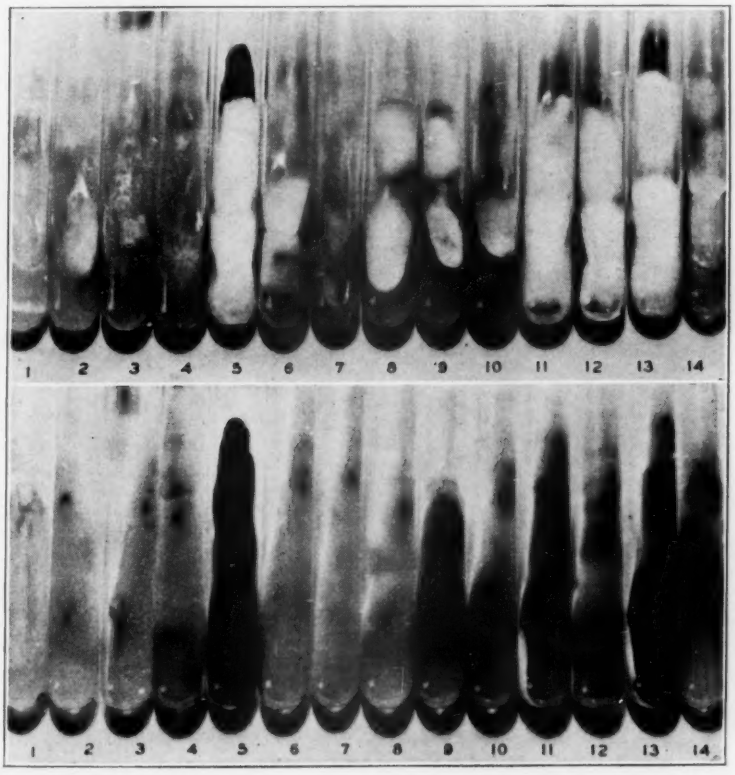

Fig. 5.—M. lanosum grown on fourteen different mediums containing the sugars in the order mentioned in the text. Pigment formed only in the tubes containing (*12*) crude dextrose, (*13*) honey, (*14*) karo, (*11*) pure dextrose, (*10*) levulose, (*9*) mannose, (*8*) mannite and (*5*) crude maltose. Starch medium is not shown.

5. A comparative study of various available carbohydrates was then undertaken. Mediums were made using Difco peptone with the following carbohydrates: (1) inulin, (2) raffinose, (3) sucrose, (4) pure maltose, (5) crude maltose, (6) lactose, (7) galactose, (8) mannitol, (9) mannose, (10) levulose, (11) pure dextrose, (12) crude dextrose, (13) honey, (14) corn syrup (karo) and (15) starch. The results showed pigment production when the following sugars were present in the culture medium: crude maltose, mannitol, mannose, levulose, pure dextrose, crude dextrose, honey and corn syrup. No pigment was

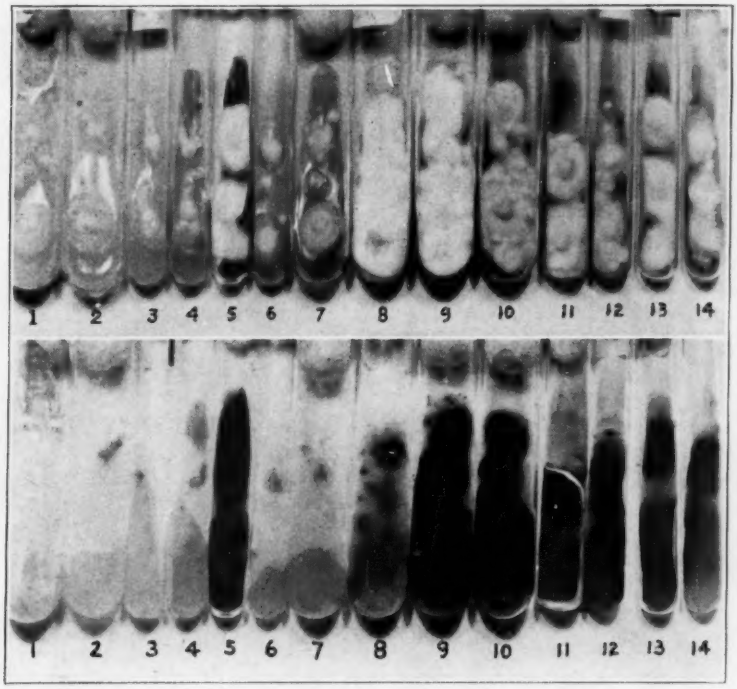

Fig. 6.—T. purpureum grown on fourteen different mediums containing the sugars in the order mentioned in the text. The same results were obtained as noted in the legend for figure 5.

formed when the following sugars were utilized: inulin, raffinose, sucrose, pure maltose, lactose, galactose and starch (figs. 5 and 6). While there was some variation in the features of the cultural growths, satisfactory results with the exception of tinctorial changes were obtained when any of the carbohydrates were used. It is of interest that with the fungi studied, pigment appeared in mediums containing three of four monosaccharides which were tried. With one exception (mannitol), disaccharides, a trisaccharide and two polysaccharides could not be utilized.

6. Inoculations were made at room temperature on agar in which lactose was the only sugar. Pigment failed to develop. Two successive transfers were made, the colonies being kept on this medium for three months. Inoculations were then made on dextrose agar when the characteristic pigment was again produced.

7. Biotin supplied by Dr. du Vigneaud, of the department of biochemistry, was added to lactose and pure maltose mediums in strengths

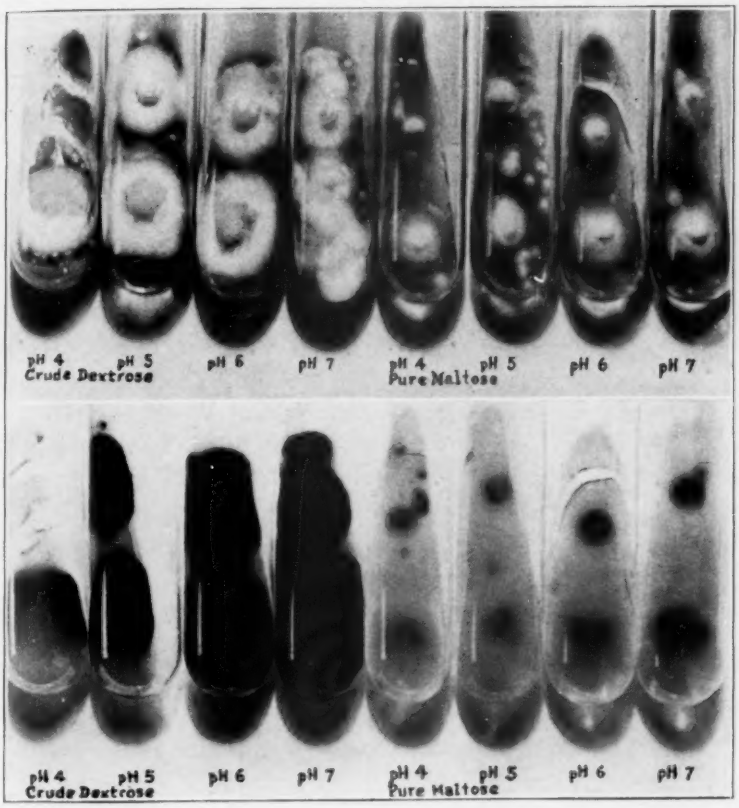

Fig. 7.—Changes in the p_H of the medium does not interfere with the formation of pigment in the tubes containing crude dextrose. No increase of pigment was noted in any medium containing pure maltose.

from 0.01 up to 1 microgram per hundred cubic centimeters. This had no effect on the development of pigment. Vitamins, including vitamins A, B_1 (thiamine hydrochloride), G, or B_2 (riboflavin), B complex, C and D, were also incorporated in the medium, but no production of pigment resulted.

8. The reaction of mediums containing crude dextrose and mediums containing pure maltose was varied in levels of p_H 4, 5, 6 and 7. No difference in the formation of pigment was noted, although the size

and texture of the growth varied somewhat. In all tubes containing crude dextrose the pigment was present, and in the tubes in which the only sugar was pure maltose no pigment developed, irrespective of the reaction (fig. 7).

9. The typical color of fungi when examined under filtered ultraviolet rays was unchanged irrespective of the composition of the medium on which it was growing. However, when the medium was such that pigment in the substrate was noticed in ordinary light, a fluorescent color could also be noticed. With T. purpureum the visible pigment in the substrate appeared a deep blue-violet. The remainder of the medium was bright light blue. With M. lanosum the pigment was a deep olive drab; there was no dispersal of color in the remainder of the medium.

SUMMARY

1. Pigment formed in the culture medium by certain fungi, such as T. purpureum and M. lanosum, is apparently a metabolic product and is not to be confused with the typical color of a species, such as the black color to be seen throughout a colony of H. pedrosoi.

2. In a colony of T. purpureum in which a spontaneous sector developed pigment was produced adjacent to the sector but in decreased amounts under the remainder of the colony. When samples of these parts of the colony were transplanted, heavy pigment was noted in the substrate of the colony which developed from the sector; in the other specimen no pigment developed.

3. The presence of agar or of peptone in the culture medium was not necessary for the development of pigment.

4. Fungi were found to synthesize pigment in the presence of certain monosaccharides with closely related structural formulas, such as dextrose, levulose and mannose. Only one disaccharide, mannitol, was useful.

5. Pigment was not produced when the only sugars in the culture medium were galactose (a monosaccharide) and disaccharides, such as maltose, sucrose and lactose. Raffinose (a trisaccharide) and starch and inulin (polysaccharides) also gave negative results.

6. It was determined that colonies which had lost their ability to produce pigment while on a lactose agar regained their chromogenic power when transfers were made to a dextrose agar.

7. The addition of biotin or of various vitamins did not enable T. purpureum to form pigment while on a lactose medium. Changing the p_H similarly had no effect.

8. Under filtered ultraviolet radiation the exogenous pigment of T. purpureum showed a deep blue-violet. The remainder of the medium gave off a bright light blue fluorescence. With M. lanosum the color of the pigment was revealed as a deep olive drab.

ABSTRACT OF DISCUSSION

DR. FRED D. WEIDMAN, Philadelphia: Twelve years ago my associates and I undertook in our laboratory an inquiry into the effects of the various ingredients of the culture mediums for the fungi which cause ringworm and conducted studies both on the peptones and on the carbohydrates. Our studies were directed toward reproducing Sabouraud's medium, or at least producing a substitute for it. In that connection, of course, color was but one of the characters concerned; we were interested also in the voluminousness, the surface configuration and the texture of the colony. In those studies color was notably influenced by the different forms of peptone. As I recall, there is some discrepancy between our work and that of Drs. Lewis and Hopper in regard to Difco peptone. The latter was not a proper substitute for the original Chassaing brand. We finally decided that Fairchild's was the most acceptable substitute, as has Dr. Lewis in his studies.

We worked with Microsporon lanosum and Microsporon equinum as our test specimens, but not with Trichophyton purpureum. Fairchild's peptone was a satisfactory substitute in connection with these. We also worked with Microsporon felineum. With this Fairchild's peptone was not at all satisfactory for the proper development of color—at least with our strain. It induced a yellow color in the colony instead of the pink which should be induced. I do not know whether Dr. Lewis included. M. felineum in his studies or not.

Since the physiologic characteristics of fungi are variable and peptones are highly variable in their composition (peptones are not pure substances; they are mixtures of proteoses, amino acids and peptones), this subject will have to be tested from time to time, as the occasion arises. The methods of manufacture of the peptones change, and with these changes the chemical composition is altered. Such a change is bound to influence the metabolism of the fungi and result in changes in the character of the colony.

Accordingly, there is no question as to the value of this presentation. The authors have shown the status of the peptones of today in regard to color production. They have succeeded in showing how the color of these colonies can be accentuated and how, even in the absence of Chassaing's peptone, there is still available the factor of color in the determination of the species.

DR. JOHN G. DOWNING, Boston: In 1936 at the Atlantic City meeting of the American Medical Association, I had an exhibit in collaboration with Miss Cousins (Mrs. Wesley Tiffney). At that time she exhibited a series of subcultures from single spore transplants, and she produced marked variation in color and size. The most striking results were found in the genus microsporon, particularly in Microsporon gypseum, and to a lesser extent in Microsporon canis (M. lanosum). Variants often appear spontaneously in old cultures of these fungi. By means of single spore transplants these variants were shown to maintain definite, constant cultural and microscopic characteristics, strikingly different from those of the parent strains, through a considerable number of subcultures. The variants differed from their parent strains in the size, color and surface texture of the colonies. For instance, M. gypseum, which typically produces a light ochraceous buff-colored colony on peptone-dextrose agar, gave rise to a number of variants which on the same medium produced colonies that were pink, light buff, yellow, mahogany red, vine red and white, respectively. The microscopic differences observed were even more striking. The fuseaux of M. gypseum were typically 44 to 52 microns long and fusiform, with an echinulate surface and five regularly spaced septums. They were borne on slender sporophores and were freed by the separation of the basal wall of the fuseau and the apical wall of the

sporophore. From this species were obtained variants in which the fuseaux ranged from 28 to 44 microns long, were subcylindric or subconical and had a smooth surface and one to five irregularly spaced septums. They were borne on sporophores greatly enlarged at the apex and were freed by the disintegration of the apical cell of the sporophore. Other variants were obtained from this same species which produced abortive fuseaux or none at all. In this work one standard medium was used to facilitate comparisons of the species and their variants.

Dr. Lee McCarthy, Washington, D. C.: I should like to ask Dr. Lewis whether he made any experiments on growth at different temperatures and whether there is any difference in the production of pigment depending on the rapidity of growth. I made some experiments with Trichophyton violaceum at one time and found that the production of pigment depended on the percentage of sugar in the medium.

Dr. George M. Lewis, New York: The studies of Dr. Weidman and his associates have shown the importance of peptones in the variations of cultural growths which may occur. From our work, it would seem that the sugar content of the medium is of more importance in so far as the production of pigment is concerned. It is of interest that one of the manufacturers of mediums uses pure maltose in the product sold as Sabouraud's agar. The use of this commercial medium explains why some investigators have been unable to reproduce the color which is characteristic for certain fungi, such as T. purpureum. Had the manufacturer used any of the monosaccharides in place of pure maltose the correct color would have been obtained. In answer to Dr. McCarthy, we made preliminary studies on the effect of variation in temperature, but we did not pursue that phase further because there were no leads. I cannot answer his question about the rapidity of growth having any influence on the formation of pigment. We have not yet a full explanation for the formation of pigment by fungi but hope to work further on the problem, in collaboration with the department of biochemistry at Cornell University Medical College.

Clinical Notes

GENERALIZED DERMATITIS FROM NAIL POLISH

HAROLD SHELLOW, M.D., CHICAGO

Dermatitis due to nail polish, though sparingly reported in the literature, is not uncommon in the experience of the dermatologist. Recently several reports have been published in *The Journal of the American Medical Association.* In the main they have concerned the occurrence of an eruption on the face and neck. In the report by Ellis and Kirby-Smith [1] 1 patient had an involvement of the shoulders and 1 had an eruption on the legs, which was due to the application of nail polish to the stocking to prevent runs. In 2 others the anterior axillary fold and the cubital fossa were affected. In the cases reported by Hollander [2] the face and neck were solely affected. In another instance [3] the chest and arms were involved.

To show that this form of cosmetic can produce an eruption of a more extensive character, I wish to report the following case.

REPORT OF A CASE

A woman about 60 years old stated that her eruption started while she was out of town about six weeks prior to her first visit to me. It began on the side of the neck and was followed in several days by the development of new patches on the neck, the face, the ears and the upper part of the chest and of the back. The eruption was accompanied by swelling, itching and weeping of the affected parts. After a short exposure to the sun these symptoms became exaggerated. She went to a dermatologist, who gave her patch tests with the cosmetics she had been using, all of which elicited negative results. With the use of soothing wet dressings and ointments the acuteness subsided somewhat, but about one week later all the previously affected parts flared up and new areas of involvement appeared. Such flare-ups occurred a number of times.

At the time of her initial visit to me, she exhibited an erythematous and edematous papulovesicular scaling and crusted dermatitis involving the face, the neck, the ears, the scalp and the upper part of the chest and of the back in ill defined patches from the size of a coin to half that of a palm. Moderate lichenification existed in the folds of the neck and in the postauricular areas. All cosmetics and soaps were eliminated from use; bland topical medication was prescribed, and fractional doses of roentgen rays were given to allay the intense itching in the lichenified parts. Her condition improved somewhat in certain areas but was unchanged in others. Injections of sodium thiosulfate and strontium bromide were given intravenously, and despite added precautions in avoiding all sorts of extraneous contacts, not only did her condition not improve on the whole but new sites of involvement developed. In ten weeks of observation her skin had become better and worse, the course being characterized by these

1. Ellis, F. A., and Kirby-Smith, H.: Contact Dermatitis Due to Nail Polish, J. A. M. A. **116**:45 (Jan. 4) 1941.

2. Hollander, L.: Nail Lacquer Dermatitis, J. A. M. A. **115**:1714 (Nov. 16) 1940.

3. Sulzberger, M. B.: Eczema Venenatum from Nail Polish, Arch. Dermat. & Syph. **42**:218 (July) 1940.

repeated flare-ups. At the peak of her eruption, in addition to the aforementioned areas, large patches of dermatitis developed on the lower part of the chest, the abdomen, the forearm, the inner surfaces of the thighs and the buttocks and in the entire axillary regions, including the arms and cubital fossa.

One day her daughter offered the information that she thought her mother became distinctly worse on the days when her finger nails were manicured. This was the only cosmetic the patient had indulged in since the onset of her eruption, and this agent had been completely overlooked as a possible source of her dermatitis. She had used a new shade of a well known nail enamel prior to leaving town and had continued its use weekly ever since.

The lacquer was immediately removed from the nails. Two test patches were applied to the skin of the back, one to be in contact for twenty-four hours and the other for forty-eight hours. The patient said that about four hours later the sites began to itch and burn. The twenty-four hour patch showed erythema and vesiculation, whereas the forty-eight hour patch showed erythema, edema and vesiculation with crusting in small central points. Sensitization was so great that the reaction extended over ½ inch (1.3 cm.) beyond the edge of the patch. Six days after the removal of the polish from the nails, the dermatitis showed a startling improvement. All the patches were fading, and the itching had become almost negligible. Without the use of medication except a bland ointment, the eruption continued to undergo involution rapidly and steadily, and in seventeen days after the removal of the nail polish it had completely disappeared, leaving no traces. The reaction to the patch tests had remained positive for nine days after application.

COMMENT

It has been stressed that investigation be made of nail polish used by women with eruptions on the face and neck of unknown causation. Unfortunately, however, no mention has been made of the possible widespread nature or generalization of such a dermatitis. Conceivably, a sensitized person may have involvement on any part of the body, wherever contact is made between skin and nails. Although no report has been recorded heretofore of an extensive dermatitis from nail polish, the incidence of occurrence of such a condition must be greater than was supposed.

Contact dermatitis from this form of cosmetic should not defy recognition, as was the case in my report, because of its generalized nature. Bearing this agent in mind as the possible causative factor may clear up the mystery in many cases of extensive dermatitis of apparently unknown cause. It is even plausible that dermatitis of vague causation in men could be attributed to sensitization to the nail polish on the fingers or even the toe nails of their mates. It is reasonably certain that since the incidence (or recognition) of nail polish dermatitis has increased, such a condition in men, as in women, will not be infrequent.

Some dyes which are contained in nail polishes are known to produce a photosensitizing effect on the skin when exposed to actinic rays. It is worthy of mention that in the case described here this may well have accounted for the original flare-up which occurred after exposure to the sun, although the patient did not permit further investigation of this sort.

SUMMARY

A case of generalized dermatitis proved to be due to sensitization to nail polish is described. It is suggested to bear this cosmetic in mind in cases of extensive dermatitis of unknown cause not only in women but even in men who contact their mates' finger or toe nails.

185 North Wabash Avenue.

RECURRENT LYMPHANGITIS TREATED WITH SULFANILAMIDE

Further Observations on a Case

S. R. Mercer, M.D., Fort Wayne, Ind.

Four years ago I treated a woman with recurrent lymphangitis with sulfanilamide.[1] It is fitting that further observations of this case should be recorded, particularly since it was the first one of chronic lymphangitis of the upper lip reported in which sulfanilamide therapy was used.

The lip is now entirely normal in size, having become progressively smaller and softer during the past two years. No exacerbations such as were formerly experienced have been noted on exposure to sunlight, on smoking of cigarets, during rainy weather or on exposure to the fumes of paint. The ingestion of alcoholic drinks continues to cause a mild transient enlargement.

A slight swelling of the lip has taken place approximately eight times. Each attack has been accompanied by a cold, and each time the swelling (an enlargement estimated to be approximately one tenth of the normal size of the lip) has been promptly controlled by the ingestion of 2 or 3 tablets (10 to 15 grains [0.65 to 1 Gm.]) of the drug one to three times a day, usually for only one day. On two occasions the patient recalls having taken the drug for the greater part of two days to control the inflammation. The total number of tablets taken over the entire period is estimated to be about 60. Again it can be stated that no untoward reaction from the drug has been noted.

The improvement has been so permanent that the patient's relatives and close friends have long ceased to comment on the condition and in fact the patient herself states that only the onset of a cold brings to mind the condition which was at one time so evident.

SUMMARY

Further improvement in a case of recurrent lymphangitis treated by sulfanilamide is reported.

710 Wayne Pharmacal Building.

1. Mercer, S. R.: Recurrent Lymphangitis Treated with Sulfanilamide, Arch. Dermat. & Syph. **39**:1042-1043 (June) 1939.

DERMATITIS DUE TO INK ERADICATOR AND COSMETIC LACQUERS

John G. Downing, M.D., Boston

F. M., a woman aged 40, was first seen by me on April 24, 1941, when she applied for treatment of dermatitis which had occurred periodically on the left side of the face during the past year. The eruption consisted of erythema and fine papules on the ramus of the left jaw and on the eyelids.

After the suggestion was made that the condition might be due to the highly colored nail polish she wore, she recalled an incident which had occurred prior

to the onset of the dermatitis. While at work she spilled a bottle of ink eradicator and noted at the time that the odor was the same as that of nail polish. After mopping up the fluid with a cloth, she noted itching of the face.

Patch tests were made with the aforementioned fluid and with face powder, rouge, lipstick and nail polish. Erythema and papules appeared at the sites of the patch tests with nail polish and ink remover. With soothing applications her dermatitis was promptly relieved.

On June 9 her hair was set and dried and was then sprayed with a lacquer-like substance to maintain the new "up-do" style. That night she suffered from severe itching and redness of the sides of the face. Subsequent patch tests with the lacquer-like substance and with acetone elicited positive reactions, the former eliciting stronger reactions. Although I am unable at present to determine the exact ingredients, apparently the substances she contacted are chemically similar.

Correspondence

SULFATHIAZOLE IN THE TREATMENT OF CHANCROIDAL INFECTION

To the Editor:—In the June issue of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (**43**:992, 1941) is an article by Glicklich and Sherman entitled "Toxic Effects of Sulfathiazole Used in Treatment of Chancroidal Infection," describing serious manifestations which occurred when 6 Gm. of sulfathiazole was administered daily for seven days and, after a short interval when treatment was suspended owing to toxic manifestations, 1 Gm. every six hours was given for a short period before the patient's condition required discontinuance of administration of sulfathiazole.

It may be pertinent to note that 6 Gm. per day is about three times and 4 Gm. per day (1 Gm. every six hours) about twice the necessary therapeutic dose of sulfathiazole. It is therefore not surprising that serious toxic manifestations occurred. The experience of Glicklich and Sherman should not discourage physicians in the use of sulfathiazole in proper doses. Chancroid yields surely and quickly to treatment with sulfathiazole, which in doses of 2 Gm. per day (0.5 Gm. every four hours for four doses) is almost without toxic effects.

CHARLES WALTER CLARKE, M.D., New York.

News and Comment

AMERICAN MEDICAL ASSOCIATION, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Applications are now being received for places on the program of the Section on Dermatology and Syphilology of the American Medical Association for the meeting to be held at Atlantic City, N. J., June 8 to 12, 1942. All Fellows of the American Medical Association are eligible. Essayists who are not Fellows may be accepted by invitation. The program is usually assembled in the early part of December.

All applications should be addressed to Dr. Nelson Paul Anderson, Secretary of the Section on Dermatology and Syphilology, 2007 Wilshire Boulevard, Los Angeles.

Obituaries

ELMORE BERNARD TAUBER, M.D.
1879–1941

Elmore Bernard Tauber, professor of dermatology and syphilology in the University of Cincinnati College of Medicine, died on June 23, 1941, after a short illness. He was born on May 4, 1879, in Cincinnati, the son of Dr. Bernard and Mrs. Hannah Kahn Tauber.

Since he was possessed of an inquiring mind and influenced by his close association with his father, it was natural that after completing his general education by taking the degree of B.A. at Oxford University, England, Tauber should enter on the study of medicine. He matriculated in the Medical College of Ohio, a forerunner by fifty-one years of the University of Cincinnati, with which institution it eventually became affiliated. He graduated and registered for the practice of medicine in 1902.

During the course of his medical studies Tauber came directly under the influence of Dr. Augustus Ravogli, who at that time was teaching and practicing dermatology, syphilology and urology. As a result of this contact Tauber did not take up the special branch of medicine of his father (who, I learned from Dr. Philip Zenner, emeritus professor of neurology, was the first practitioner and professor of laryngology in Cincinnati) but became interested in Dr. Ravogli's specialty. As a consequence of this impetus he assisted his teacher for some time in his extensive office practice. After this period of practical introduction Tauber devoted some time to study at the fountainheads of dermatologic and syphilologic knowledge in New York, Vienna, Hamburg and London, where, thanks to the letters of introduction from his preceptor, Dr. Ravogli, he was accorded special opportunities.

Interrupting the chronologic sequence of Tauber's curriculum vitae, I mention here that his European contacts were maintained through annual pilgrimages to the shrines of dermatologic study and through regular attendance at international congresses.

On his return to Cincinnati, Tauber served in various teaching positions and after the death of Dr. Meyer L. Heidingsfeld (1918) was appointed professor of dermatology and syphilology and director of the correlated services of the Cincinnati General, Children's and Jewish hospitals, positions in which he continued until he died. Dr. Tauber was a member of the Cincinnati Dermatological Society and one of the founders of the Central States Dermatological Association. In 1930 he

served as chairman of the Section on Dermatology and Syphilology of the American Medical Association, and in 1931 he was elected a member of the American Dermatological Association. He was also a member of the Co-ordinating Committee of the Public Health Federation and was

ELMORE BERNARD TAUBER, M.D.
1879–1941

treasurer of the Tenth International Congress of Dermatology, which was postponed on account of the war.

Tauber's publications and addresses mirror his unflagging active interest in the progress of the various aspects of his chosen branch of medicine. His first paper was "Observation and Treatment of Chronic

Gonorrhea," dealing with a venereal disease in which his teacher Ravogli always was interested. Several publications by Tauber and his clinical collaborators report their investigations of the treatment of burns.

Tauber's last publication (*Med. Bull. Univ. Cincinnati* **8:** 55-65 [Feb.] 1941), which appeared a short time before his death, presents "a synopsis of medical and lay contributions, stating our profession's position in the social, physical and economic structure of today." Perusal of the discourse reveals that the synopsis—bearing the title, "The Dermatologist Looks at Medicine"—is based on lifelong keen observation of the scientific and sociologic development of medicine. Tauber's philosophic reflections leave one with the impression that they were composed as a valedictory message to his colleagues and friends under the influence of a psychic premonition of his impending, untimely demise.

The painful emotion caused by Dr. Tauber's unexpected death makes it hard to assess the loss incurred by his friends and associates. Extensive practical experience, commensurate knowledge of medical teachings and abhorrence of ultramodernistic therapeutic fads, coupled with the common sense of a clear mind, were the dominant characteristics guiding him in his professional ministrations. A certain grim austerity and abruptness of manner and a fervid expression of his displeasure were sometimes evoked by incidences of which he disapproved.

With Mrs. Tauber, his only complete intimate, as a charmingly genial and gracious hostess, Dr. Tauber often entertained local and visiting colleagues. He was a valued member in several clubs and fraternal organizations, including the Omega Upsilon Phi fraternity.

Dr. Tauber's life was rich in accomplishment and achievement and made happy by a wide variety of interests. Of these interests his judicious bibliophily provided an abundance of both pleasure and information to his friends, who were allowed free access to his collection of precious literary and medical treasures.

KARL G. ZWICK, M.D.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

ISOLATED RHEUMATIC NODULE OF THE UPPER EYELID. J. S. GUYTON and J. M. McLEAN, Am. J. Ophth. **220**:985 (Sept.) 1939.

Guyton and McLean report 2 cases of nodule of the upper lid. They give the following summary and conclusions:

"Two cases are reported in Negro children, both of whom show isolated subcutaneous nodular inflammatory tumors, in the region of the upper lid and brow, of the histologic nature of 'rheumatic' nodules. As the review of the literature indicates, such nodules may be: (1) the sole manifestation of rheumatic fever, (2) a form of either syphilis or yaws, (3) an accompaniment of rheumatoid arthritis, or (4) a subcutaneous form of granuloma annulare. Since all but the first and last possibilities can be definitely ruled out in our cases, we are forced to conclude that they represent either a manifestation of rheumatic fever or the subcutaneous variety of granuloma annulare—which, after all, may be one and the same thing."

W. S. REESE. [ARCH. OPHTH.]

ACUTE GINGIVOSTOMATITIS IN CHILDREN. J. D. MCKINNEY, Illinois M. J. **77**:269 (March) 1940.

Acute gingivostomatitis is a definite disease entity occurring in a definite age group. Attempts to state its cause have resulted in considerable controversy. Its infectious character has not been proved. The rapid course of the disease is against any theory that the cause is a deficiency. There seems to be a seasonal appearance of the disease. Its course follows a rather definite pattern, and complications or sequelae are rare. Treatments of various types have been described, but none has proved to have specific value.

BARBOUR, Peoria, Ill. [Am. J. Dis. Child.]

STUDIES OF THE ANTIBODIES IN HUMAN HYPERSENSITIVENESS. ROBERT A. COOKE and WILLIAM B. SHERMAN, J. Bact. **39**:62 (Jan.) 1940.

Studies were made by the authors "on the specificity of the skin-sensitizing antibodies found in the natural sensitizations of man, the presence of a 'blocking' antibody following injections of antigen in such cases and the specificity of this blocking antibody. The method of passive transfer used consists in injecting sensitizing serum into the skin of nonreacting human subjects. After the lapse of 2 days, the sites are tested with antigen. The sensitizing antibody may be neutralized by the addition of sufficient antigen to the serum before injection.

"In cases of human sensitization, multiple reactions as determined by passive transfer are frequent. Using serum from such cases, one antigen often effects neutralization of biologically unrelated antigens. The dominant antigen in the neutralization is usually the one to which the individual is clinically most sensitive. There is evidence of the existence of a blocking antibody which results from the specific injection."

The observations are most interesting, and the authors raise the question "whether the skin-sensitizing antibodies found in human hypersensitiveness are produced solely by antigenic contacts. Certainly, as far as they have been investigated, their specificities do not conform to those of antibody produced in normal animals or man by the injection of antigen."

CHARACTERISTICS OF FUNGOUS DISEASES. ARTHUR T. HENRICI, J. Bact. **39**:113 (Feb.) 1940.

The author submits "as the outstanding characteristic of the fungous diseases their marked tendency to give rise to hypersensitivity of a type best designated as the allergy of infection, distinct from other categories of hypersensitivity." He believes "that the other characteristics of the mycoses, age and occupational incidence, course and pathology, are strongly colored by or dependent upon this allergy. This characteristic distinguishes the fungous diseases from most of the other microbic diseases, but closely relates them to tuberculosis, and in some aspects to leprosy, syphilis, glanders, tularemia and lymphogranuloma inguinale. These diseases present a common problem in immunology more or less peculiar to themselves." The author suggests "that this characteristic is determined by the ability of the pathogenic fungi and related microbes to produce peculiar antigen-like substances having specific properties not common to all antigens, and that the deep seated mycoses are caused by occasional species of saprophytic fungi which, evolving in restricted areas, have by chance acquired the ability to synthesize such substances."

STOESSER, Minneapolis. [AM. J. DIS. CHILD.]

ERYTHEMA INFECTIOSUM: CLINICAL OBSERVATIONS DURING AN EPIDEMIC. J. M. RECTOR, J. Pediat. **15**:540 (Oct.) 1939.

The author reports 43 cases of erythema infectiosum observed during an epidemic in San Francisco during the spring and summer of 1938. The constitutional symptoms were slight. The salient feature of the disease was the rash, which usually made an initial appearance on the cheeks and occurred as rose red maculopapules that rapidly coalesced into a confluent mass with a symmetric butterfly configuration. The nasolabial region was not involved, giving the appearance of circumoral pallor. Within twenty-four to thirty-six hours the rash developed on the trunk and extremities. On the trunk it appeared as a fine discrete maculopapular eruption, practically indistinguishable from German measles. On the extremities the rash was more marked on the extensor surfaces, where it occurred as large macules or maculopapules that assumed a violaceous tinge. These faded from the center and left well defined peripheries forming characteristic gyrate patterns. The buttocks showed a similar distribution. The eruption disappeared rapidly from the face and trunk but in some cases lasted six to fourteen days on the extremities, fading for hours or days and then reappearing.

RAUH, Cincinnati. [AM. J. DIS. CHILD.]

NOTES ON SCLERODERMA (DERMATOMYOSITIS). T. LEWIS, Brit. J. Dermat. **52**:233 (Aug.-Sept.) 1940.

Lewis reports a case of fatal scleroderma in which early manifestations consisted of circulatory disturbances in the fingers complicated by multiple thromboses in the digital arteries. After a period of quiescence scleroderma developed rapidly, affecting the feet, hands (sclerodactylia) and face, associated with bodily wasting and with changes in the muscles "regarded as characteristic of those found in so-called dermatomyositis." Detailed postmortem observations are recorded. The muscle changes consisted of atrophy of fibers, increase of sarcolemma nuclei and proliferation of interstitial connective tissue. Lewis believes that diffuse scleroderma is perhaps primarily a subacute or chronic inflammatory disease, and he discusses a concept of the unity of dermatomyositis and diffuse scleroderma.

GENERALIZED SCLERODERMA. G. B. DOWLING, Brit. J. Dermat. **52**:242 (Aug.-Sept.) 1940.

The author postulates the "identity" of progressive scleroderma with dermatomyositis and suggests a relation of both these diseases with disturbances of the thyroid gland. He believes that their cutaneous features, Raynaud phenomena and

clinical course indicate that dermatomyositis and scleroderma are but varying aspects of the same process. A resemblance is seen between the histopathologic changes in the muscles of dermatomyositis or scleroderma (collections of lymphocytes and atrophy of muscle fibers) and the lymphorrhages of thyrotoxicosis. Clinically, Dowling considers that the chronic thyrotoxic myopathy corresponds with the myopathy of scleroderma or dermatomyositis. The thyroid in scleroderma is said to be the seat of pathologic alterations, and in 2 patients with conditions diagnosed as dermatomyositis by Dowling histologic abnormalities of the thyroid were present. These observations, together with the creatinuria as well as disturbances in carbohydrate and calcium metabolism occurring in progressive scleroderma and in many cases of goiter, suggest to the author the possibility of an etiologic link between the thyroid gland and scleroderma or dermatomyositis.

GENERALIZED SCLERODERMA AND DERMATOMYOSITIS: A HISTOLOGICAL COMPARISON. W. FREUDENTHAL, Brit. J. Dermat. **52**:289 (Oct.) 1940.

Freudenthal's material was obtained from 11 cases of dermatomyositis and 4 cases of progressive scleroderma with muscle changes. In dermatomyositis, the cutis, after an edematous stage, becomes increasingly sclerotic and atrophic, and the epidermis secondarily becomes thinned and flattened. The variety of muscular changes in dermatomyositis is described. The muscle, after an initial edematous phase, undergoes degenerative changes; the perimysium proliferates, and some inflammatory reaction is present. Lymphorrhages (focal collections of round cells in the muscle) occurred in 3 cases of dermatomyositis and in 1 of scleroderma. "They link up generalized scleroderma and dermatomyositis with Graves's disease and myasthenia gravis." The author could find no essential difference between the changes in the skin and muscle of dermatomyositis and those of generalized scleroderma.

BIOCHEMICAL ASPECTS OF DERMATOMYOSITIS. W. J. GRIFFITHS, Brit. J. Dermat. **52**:295 (Oct.) 1940.

Certain metabolic aspects of dermatomyositis show a close similarity to those of endocrine (thyroid and pituitary) disease. Thus creatinuria occurs in both conditions, as do also alterations in carbohydrate metabolism. Griffiths observed a distinct interference with the action of insulin on the muscles in dermatomyositis by observing the difference of concentration of dextrose in arterial and venous blood of an extremity. Normally dextrose is removed from the blood by the muscles, with the result that the blood leaving the extremity contains less sugar than that entering it. A diminished arteriovenous difference ensues when the muscles fail to increase their uptake of sugar from the blood, a circumstance observed to occur in dermatomyositis. From these observations it is reasoned that there is interference with the formation of muscle glycogen in dermatomyositis, which leads to the appearance of creatine in the urine.

Other biochemical changes noted in dermatomyositis were fluctuations in the amount of creatinine excreted, signs of decalcification of the bones and a tendency for the sodium of the blood plasma to be low.

RETICULOENDOTHELIOSIS AND NORMOBLASTOSIS. F. S. P. VAN BUCHEM and T. BOTMAN, Brit. J. Dermat. **52**:304 (Oct.) 1940.

A woman aged 31 had an extensive nodular eruption with generalized lymphadenopathy. Hematologic examination revealed anemia, 7,400 leukocytes per cubic millimeter of blood and, later, as many as 88 normoblasts per hundred leukocytes. Biopsy of a specimen of a cutaneous nodule disclosed focal proliferation of polymorphous reticuloendothelial cells about the subcutaneous capillaries. Similar changes were observed in a lymph node and in bone marrow, where, in addition, large numbers of normoblasts were present. The patient died after an illness of ten weeks.

At necropsy it was ascertained that the initial reticuloendotheliosis had developed into a picture of Hodgkin's disease. The spleen was shrunken. There was no evidence of extramedullary hemopoiesis. The authors ascribe the normoblastosis to a failure of the reticuloendothelial system. WAISMAN, Chicago.

TREATMENT OF ECZEMA WITH VITAMIN-B COMPLEX. K. P. KRISTENSEN and S. N. VENDEL, Lancet **1**:170 (Jan. 27) 1940.

The knowledge of allergy, hormones and vitamins has so far not solved the problems of the etiology, diagnosis and treatment of eczema. In a series of more than 100 unselected cases of eczema many different preparations of vitamin B complex were tried, some by mouth and some by injection. They seemed to be all equally effective against eczema. Generally, in a week or ten days the acute eczema is healed. In about one or two weeks the chronic condition is definitely better. Although the factor concerned in the cause and cure of eczema in all probability resides in the vitamin B_2 (G) complex, the authors obtained excellent results from the administration of the whole vitamin B complex.

LUPUS ERYTHEMATOSUS: THE EFFECTS OF SULFONAMIDES. H. W. BARBER, Lancet **1**:583 (March 30) 1940.

In most of the cases of lupus erythematosus met with in England the condition is, in the belief of Barber, of streptococcic origin; in some cases the eruption may be a toxituberculid. When the disease has been apparently due to streptococcic infection, characteristic reactions to treatment with sulfanilamide and its derivatives have been observed, with subsequent benefit to the eruption in a high percentage of cases, whereas when a tuberculous infection was apparently responsible these reactions did not occur nor was the eruption affected.

LANGMANN, New York. [AM. J. DIS. CHILD.]

SOME BASIC PRINCIPLES IN LEPROSY TREATMENT. E. MUIR, Leprosy Rev. **11**: 162 (Oct.) 1940.

Leprosy occurs in two forms: the more severe type and the milder, localized type, which is often abortive. The form depends on the response to infection of tissue cells, or histiocytes. If they react to the infection by decided proliferation, epithelioid cell tubercles form, which either destroy or inhibit the growth of the bacilli. If the tissue reaction is mild (lepromatous reaction), the bacilli survive and multiply and may even travel to other sites.

The treatment of leprosy aims at two objectives: to strengthen and stimulate the cells to act more vigorously and to break down the defense of the bacilli.

1. *Stimulation and Strengthening of the Tissue Cells.*—The cause of differences in individual response to infection is not understood. The general health of the patient surely affects his resistance to disease. Deterioration of health may lead to the degeneration of less serious tuberculoid lesions into the more severe lepromatous type with its lack of cellular reaction. Many forms of treatment probably function by stimulating local cellular activity and the mobilization of phagocytic cells about the lesions, for instance, ironing the skin and applying trichloroacetic acid to the lesions. Chaulmoogra oil injected into the cutaneous lesions stimulates the cells locally. Active physical exercise improves the metabolism and general health.

2. *Breaking Down Bacillary Defense.*—This reaction is most evident in the lepromatous type of tissue response and leads to the formation of lepromatous lesions, with (*a*) the encapsulation of the bacilli in a protective connective tissue wall where they are retained uninjured, (*b*) the obstruction by bacilli of lymphatic spaces through which curative medicaments might otherwise reach them and (*c*) the formation of a protective wall consisting of a mucoid mass of dead and swollen bacilli making the bacilli dwelling within this mass impervious to watery fluids. External applications and exercise help break down this triple defense mechanism

of the bacilli, so as to bring them slowly into contact with tissue cells. Iodides aid in breaking down bacillary defense but are extremely dangerous unless used cautiously in carefully selected persons in comparatively good health.

Large doses of dyes may cause evacuation of leproma but with such severe accompanying reactions that their employment is dangerous. Attempts at immunization in lepromatous cases by injection of lepra bacilli emulsion have been found useless. What is most required in the treatment of leprosy is a safe means of activating the tissue cells in the early stages of lepromas.

INTRANASAL TREATMENT IN LEPROSY. E. MUIR, Leprosy Rev. **11**:173 (Oct.) 1940.

One of the most distressing complications of leprosy, especially of the lepromatous type, is involvement of the nasal cavities and their sinuses. Primary involvement is usually followed by secondary infection. Treatment of this condition consists of

(*a*) the prevention of sepsis by a technic described in detail but consisting essentially of a method of displacement irrigations, (*b*) treatment of the actual sepsis by a modification of the aforementioned technic employing different solutions and a more thorough technic of irrigation and subsequent washings and (*c*) cauterization of the actual lesions with trichloroacetic acid with cocaine anesthesia.

The importance of early treatment of nasal lesions is twofold: (*a*) prevention of deformities and (*b*) lessening of the danger of discharge of the bacilli from the nose and consequent spread of the infection.

EXPERIMENTAL STUDIES ON THE COMBINED SULPHANILAMIDE AND SERUM TREATMENT OF GAS GANGRENE INFECTIONS. E. SINGER, M. J. Australia **2**:275 (Sept. 28) 1940.

In a previous communication it was demonstrated that sulfanilamide and its derivatives exhibited a weak action against Clostridium welchii and Clostridium septicum but gave no protection against infection with Clostridium oedematiens. In cases in which mice succumbed in spite of administration of one of these drugs it was found that cultures of the heart blood, liver and spleen were sterile; so death was presumably due to toxin absorption from the site of inoculation. It seemed worth while, therefore, to investigate to what extent sulfanilamide and its derivatives would protect the animals if combined with antitoxic serums.

In all experiments insufficient antitoxic serum was administered to inhibit the course of the induced infection. Depending on the amount of serum administered, the dose of the drug necessary to prevent death of the animal could be reduced to from one-half to one-eighth the dose required without the simultaneous use of antitoxic serum. These results hold for Cl. welchii and Cl. septicum infections. Attempts to treat Cl. oedematiens infection with a combination of drug and serum (the latter in insufficient quantity of itself to cure the animal) met with failure.

It is now well known that most bacterial toxins affect the adrenal glands. Experiments were carried out to demonstrate the protective effect of the administration of adrenal cortical extracts in increasing resistance to the toxin produced by the gas bacillus Cl. welchii. Desoxycorticosterone acetate administered before a fatal dose of Cl. welchii toxin protected 6 out of 8 mice so treated, as compared with only 1 survivor of 8 unprotected by previous administration of the extract.

PINK DISEASE: A CONSIDERATION OF THREE AETIOLOGICAL POSSIBILITIES. F. W. CLEMENTS, M. J. Australia **2**:430 (Nov. 2) 1940.

Three theories have recently been advanced to explain the cause of pink disease, or acrodynia.

1. The spores of a cereal smut cause the disease. Mayerhofer, in Jugoslavia, identified acrodynia with a disease produced by the ingestion of cereals infected

with a smut fungus. The author, however, was unable either by feeding experiments or by injection experiments to reproduce the toxic effects of the disease in laboratory animals by employing smut spores from Australian cereal.

2. Vitamin B_1 (thiamine) deficiency is the cause of acrodynia. While it is true that a number of different observers have demonstrated improvement in cases of acrodynia by administration of vitamin B_1, results were often temporary and were too uncertain to justify the claim that the disease is due to a vitamin deficiency. As a matter of fact, many of the infants who contract pink disease have been especially well nourished up to the time the disease sets in, and the loss of appetite characteristic of the disease together with the depletion of thiamine by heightened metabolism during the course of the disease might well account for the deficiency of the vitamin, and the resulting symptoms may be merely the consequence and not the cause of the disease.

3. Some hold that acrodynia is due to infection by a neurotropic virus. The author describes 2 cases, both in previously well nourished and healthy children from Canberra, Australia. The disease occurred after they had, at different times, visited Melbourne, Australia. The complete absence of other cases in Canberra suggests that the disease in these instances was contracted by infection while visiting in Melbourne. The author does not draw any conclusions from these cases but suggests that they offer some support for the theory of an infective organism as the cause of pink disease.

FRUMESS, Denver.

A NEW CASE OF NORWEGIAN SCABIES. J. GOLAY, Ann. de dermat.et syph. **10**: 976, 1940.

The disease occurred in a cachectic man aged 71. He was first seen in April 1939, although the eruption appeared in September 1938. Norwegian scabies was described by Boeck and Danielson among lepers in Norway. It is rare, only about 60 cases having been reported. It is characterized by a universal erythematosquamous, keratotic eruption which, in contrast to normal scabies, does not spare the face and scalp. The keratoses are distributed irregularly over the body, but as a rule the upper extremities, especially the hands, are most intensely involved. The diagnosis is difficult since, besides the keratotic lesions, there is often a polymorphous eruption composed of pustules, vesicles, excoriations, fissures and lichenified plaques. Sometimes the texture of the skin resembles that in scleroderma. There may be pigmentary disturbances resembling radiodermatitis. There may be total alopecia. The nails are always involved and seem spongy and raised by keratotic material beneath them. Burrows cannot be found as a rule, even though they are present, since they are concealed beneath the keratotic debris. Itching is usually moderate, sometimes less than in ordinary scabies. In most cases the condition is of long duration (several years).

The author's case is of special interest since the condition occurred in a man of good hygiene.

For many years Norwegian scabies was considered to be caused by a parasite of animal origin. Actually, however, as Dubreuilh showed in 1924, it is a special type of human scabies caused by Sarcoptes hominis. Certain authors have claimed that differences exist between the acari of Norwegian and those of ordinary scabies; others have stated that they are identical. In the author's case the female acari were very large. The consensus is that the terrain rather than a special kind of Sarcoptes hominis favors the development of Norwegian scabies. The disease usually occurs in debilitated or cachectic persons of poor hygiene. Persons who contract scabies from one who has the Norwegian type have the normal form of the disease.

LAYMON, Minneapolis.

RECKLINGHAUSEN'S NEUROFIBROMATOSIS, ATROPHODERMA VERMICULATA AND CONGENITAL ANOMALY OF THE HEART AS CHIEF SYMPTOMS OF A FAMILIAL SYNDROME. W. L. L. CAROL, E. G. GODFRIED, J. R. PRAKKEN and J. J. G. PRICK, Dermatologica **81**:345 (June) 1940.

A 19 year old girl and her mother had atrophoderma vermiculatum. In the daughter the disease occurred not only on the face but also on the extensor surfaces of the extremities. Besides the atrophy, numerous cysts which resembled milia were visible. Histologically there was no connection between the cysts and the hair follicles. These cysts seemed to belong to the sweat glands. They were filled with horny concentric layers of epithelium which were either solid or tubular. A mongoloid expression of the face was noted. Tumors of neurofibromatosis were present. Congenital heart block was diagnosed clinically and by means of the electrocardiogram. The patient had undergone an operation for ovarian cysts a few years before. The mother also showed atrophoderma vermiculatum, with recurrent basal cell epithelioma of the face, Recklinghausen's disease, a mongoloid facial expression, mental debility and congenital heart disease. Another daughter, 15 years old, had forme fruste of neurofibromatosis. A 7 year old son had a mongoloid expression, questionable Recklinghausen's tumor and isthmus stenosis of the heart. Other members of the family were also examined. The maternal grandfather had neurofibromatosis, and the mother's brother, kyphoscoliosis, Recklinghausen's disease and mental debility. HELEN O. CURTH, New York.

CAN PSORIASIS BE HEALED BY RESIDENCE IN THE TROPICS? ROBERT SIMON, München. med. Wchnschr. **87**:288 (March 15) 1940.

The author for some time practiced dermatology in Java. It is generally accepted that psoriasis is less frequent in the tropics than in colder climates. The average incidence in Europe is 6 per cent and in America about 3 per cent. The condition occurs rarely among Negroes and Indians. The incidence among Jews is not greater than among Aryans.

During his stay in Java the author observed psoriasis in 7 patients among 187 full-blooded Europeans in his practice and in only 3 patients among 270 with Indian or Chinese blood.

From his observations the author concludes that there is a racial factor which determines the prevalence of psoriasis. Food and sunshine are not important factors. White persons with psoriasis are not benefited by residence in the tropics. BRAHDY, Mount Vernon, N. Y. [Am. J. Dis. Child.]

THIRD GENERATION SYPHILIS. PAAVO MAIJALA, Acta med. Scandinav. **103**:1, 1940.

Maijala reports a fairly authentic case. The grandmother admitted promiscuity in her early youth but was never aware of infection. She was always in "good health." She had one stillborn child and then five premature children, of whom only one survived, a daughter, who represents the second generation. The latter was very weak and from the age of 8 years suffered from dizziness and headache, worst at night. She always tired easily. The Wassermann reaction of the serum was doubtful and that of the spinal fluid negative (syphilitic vascular disease?). She had never had extramarital intercourse; her husband stated that he did not have syphilis; his Wassermann reaction was negative, and the physical examination revealed no evidence of syphilis. Her 17 year old son represents the third generation. He had interstitial keratitis of one eye at 8 years of age and of the other at the time of his admission to the hospital. Hutchinson teeth and the positive serologic reaction gave the proof of congenital syphilis. The grandmother's serum taken at that time showed a positive reaction. Her spinal fluid

gave a positive Pandy reaction. The pupils were asymmetric and reacted sluggishly to light. With syphilitic therapy the Wassermann reactions of all 3 persons became negative and the mother's headache and fatigue disappeared.

KAJDI, Baltimore. [AM. J. DIS. CHILD.]

IS THERE A CONNECTION BETWEEN HERPES ZOSTER, VARICELLA AND SYMPATHETIC OPHTHALMIA? G. VON BAHR, Acta pædiat. **25**:1, 1939.

Herpes zoster in a 5 year old boy was followed by attacks of varicella in the 2 roommates with whom he had been isolated. The 3 patients were under treatment for perforating wounds of the cornea, in each instance involving only one eye. In the boy who had herpes and in 1 of the 2 contacts sympathetic ophthalmia developed. This complication is stated to occur only once in 10,000 cases. Although its appearance in 2 of 3 patients suffering from a coincidental traumatic lesion and a virus infection may have been fortuitous, the cases are presented as suggestive evidence of the herpetic origin of sympathetic ophthalmia. Experimental support of this possibility has been obtained by von Szily. Sommer has published 2 comparable cases.

MCCUNE, New York. [AM. J. DIS. CHILD.]

Society Transactions

NEW ENGLAND DERMATOLOGICAL SOCIETY

J. HARPER BLAISDELL, M.D., *President*

BERNARD APPEL, M.D., *Secretary*

Boston, Dec. 4, 1940

Chronic Discoid Lupus Erythematosis with Subacute Dissemination. Presented by DR. FRANCIS P. MCCARTHY, Boston.

J. M., a 30 year old man, entered the hospital on Aug. 2, 1940 with a history of an eruption, fever, malaise and pleuritic pain which had been present for three years. He was discharged on August 14 and reentered the dermatologic service on November 17 with the same complaint. In January 1932 he had had a penile lesion and lesions of secondary syphilis. The reaction to a Kahn test was positive, and he received antisyphilitic treatment from 1932 until 1935. He is known to be an alcoholic addict.

Examination reveals discoid red and brownish lesions on the face, ears and neck, with atrophy, scales, dilatation and plugging of the follicles and telangiectasia. There are several scaly erythematous maculopapular lesions on both arms. His liver is enlarged and extends 7 cm. below the costal margin. There is an icteric tint to the scleras.

The icteric index of the blood was 18 and 10. A roentgen ray examination showed an infiltrate suggestive of pneumonia in the left hilar area. He received a total of 21 Gm. of sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) within five days during the hospital period. He remained free of fever until discharged from the hospital. However, since then he has shown a slight daily elevation in his temperature.

DISCUSSION

DR. J. HARPER BLAISDELL, Boston: I should like to call attention to 2 private patients who had a rise in temperature from 99 to 100 F. every afternoon for many months. Is that consistent with discoid lupus erythematosus?

DR. E. M. STANDISH, Hartford, Conn.: I know of a patient with a subacute condition who had no fever at all. In fact, her general condition was relatively good, and she had a fairly normal white blood cell count.

DR. FRANCIS P. MCCARTHY, Boston: I saw this patient in consultation in the medical service of the hospital, and at that time the lesions were showing a tendency toward dissemination. I do not believe there have been any lesions of secondary lupus since that time. On that basis one could not definitely say that the condition is discoid lupus erythematosus. The question of visceral lesions, including endocarditis, renal lesions and the hepatic damage, entered the picture. He still has a low grade icterus. The condition of the liver probably is an alcoholic cirrhosis. He had new lesions on both arms. I am inclined to believe that he will not show any further dissemination of the disease, and I feel that his condition probably was due to excessive ingestion of alcohol prior to coming to the hospital.

A Case for Diagnosis (Bronchiectasis with Clubbed Fingers and Toes. Acral Distribution of Purpuric Lesions. Scurvy?). Presented by DR. WILLIAM P. BOARDMAN, Boston.

W. M., a man aged 58, is a known alcoholic addict, who imbibed large quantities of alcoholic liquor recently. His food intake became poor, and in the last few

months he has had little citrus fruit. He was admitted to the medical service on Nov. 2, 1940 with purpura of the nose, fingers, toes, scrotum and knees of one day's duration. On admission he showed purpuric areas on the fingers, hands, toes, knees, scrotum and nose. Chemical examination of the blood showed no vitamin C in the plasma. A tourniquet test showed twelve petechiae in 2 square inches (12.5 sq. cm.) in five minutes. At present there is only clubbing of the fingers and toes. He was treated with supplementary amounts of ascorbic acid (vitamin C), and he received the hospital diet.

DISCUSSION

DR. HAROLD J. JEGHERS (by invitation), Boston: I think the unusual point is that this man had multiple vitamin deficiency. The scurvy was interesting in that his associated vitamin B_1 deficiency produced vasodilatation which, together with the underlying bronchiectasis and resultant clubbing of the fingers, caused his purpuric lesions to have an acral distribution.

DR. FRANCIS P. MCCARTHY, Boston: Have you found a deficiency of vitamin G (B_2) in cases of chronic alcoholism?

DR. HAROLD J. JEGHERS (by invitation), Boston: I have seen several alcoholic addicts with this condition.

Multiple Vitamin Deficiency: Pellagra, Riboflavin Deficiency, Beriberi and Subclinical Vitamin A and Vitamin C Deficiency. Presented by DR. WILLIAM P. BOARDMAN, Boston.

M. G., a 30 year old woman, entered the hospital on Nov. 7, 1940 with dermatitis, nausea, vomiting and diarrhea of several weeks' duration. For the past several months she had been drinking alcoholic liquors rather steadily, at the expense of an adequate dietary intake.

Her skin was dry and presented many hyperkeratotic follicular plugs on the arms and legs. The hands and elbows presented a dry, scaly pigmented dermatitis which was symmetric. Capillaries extended from the scleras past the free limbic area, which usually is avascular, into the cornea. The lips were slightly cracked and increased in color. She showed Sebrell's lesion at the angles of the lips. There were many telangiectases on the cheeks. The nose presented a sharkskin appearance. The tongue was fiery red; the tip and lateral thirds were smooth, and the ventral surface was covered with a dense white membrane. There was hyperesthesia of the soles and pain on squeezing the calf muscles.

The blood plasma showed: carotenoids, corresponding to 7.8 U. S. P. units of vitamin A per hundred cubic centimeters; vitamin A, 15.9 U. S. P. units, and ascorbic acid (vitamin C), 0.03 mg. She was treated with nicotinic acid, 150 mg. daily. Four days later she showed remarkable improvement. The lips were almost healed; the tongue was pinkish, and the membrane was almost all gone. The skin on the hands and elbows was improving. On November 19 she received thiamine hydrochloride, liver and riboflavin, and on November 22 the lesions had practically disappeared.

Rosacea with Keratitis (Vitamin Deficiency?). Presented by DR. WILLIAM P. BOARDMAN, Boston.

On Nov. 21, 1940 R. G., a 40 year old woman, was admitted to the ophthalmic service with a history of moderate rosacea and photophobia with lacrimation. This condition had been present for several weeks. The dietary intake had been adequate.

She showed a moderately advanced rosacea of the face. The right eyelids were red and edematous, with ciliary and conjunctival injection. The cornea presented several deep grayish infiltrations. There were a small pannus at 12 o'clock, advancing about 2 mm., and fine blood vessels at the limbus. The pupil was well dilated and the anterior chamber was normal. The lens of the right eye was clear, and the media and fundus could not be examined because of photophobia.

The left eyelids were red, with no edema. There were moderate conjunctivitis and ciliary injection. There were a few infiltrates at the periphery of the cornea. The lens of the left eye was clear, and the media and fundus were not examined because of the photophobia. Analysis of the gastric contents showed no free acid and total acid amounting to 3. She was treated with riboflavin, with decided improvement.

DISCUSSION OF CASES OF VITAMIN DEFICIENCY

Dr. Harold J. Jeghers (by invitation), Boston: This 40 year old woman presents the classic features ascribed to riboflavin deficiency. Riboflavin is one of the vitamins of the vitamin B complex group and is now known to be important in maintaining proper oxidation of all body cells by virtue of its ability, after being phosphorylated, to combine with a protein to form the yellow oxidative enzyme of Warburg. Riboflavin is readily deactivated by light. This is a point of interest, since the lesions in riboflavin deficiency occur primarily on the face and in the eyes, portions of the body exposed to light. It is poorly absorbed when achlorhydria is present.

Avascular areas, such as the cornea, depend on this oxidative system entirely for proper oxidation of the cells. When riboflavin deficiency occurs, this oxidative enzyme system is no longer adequate, and capillaries grow into the cornea, with resultant keratitis. This also occurs on the face, with resultant flushing and telangiectasia. The acne lesions are probably secondary. Seborrhea is common; the skin of the nose, in the nasolabial folds and on the forehead becomes greasy with many comedos, giving the typical sharkskin appearance. The lips are cracked and red, and lesions similar to rhagades appear at the angles of the mouth. The tongue has a characteristic color (magenta), with the papillae flattened rather than atrophied. Photophobia and other ocular symptoms are common.

The first patient had pellagra, beriberi and subclinical A and G avitaminosis, as well as the riboflavin deficiency. After being given a basal diet low in all vitamins she was given nicotinic acid. All her pellagrous manifestations cleared within six days. Riboflavin was then added, with resulting rapid improvement in the keratitis, the telangiectasia of the face and the lesions on the lips. Later thiamine hydrochloride was administered, with relief of the muscular pains in the calf muscles.

The daily requirement of riboflavin is about 1 mg. Eggs, milk, liver and some of the green vegetables are the important dietary sources. Patients have been given as much as 25 mg. daily with no ill effect. However, the commercial preparations are still expensive for such large doses. Good results have followed the use of 5 to 10 mg. daily by mouth in divided doses. Riboflavin preparations suitable for intravenous or intramuscular injections are also available.

Dr. Nels A. Nelson, Boston: After the condition is improved, can that state be maintained by diet?

Dr. Harold J. Jeghers (by invitation), Boston: Yes, except possibly in persons with achlorhydria. Achlorhydria may explain why there are exacerbations. The mild condition seen in patients in the hospital usually are maintained by diet. Severe conditions with keratitis are usually seen by the ophthalmologists. The classic treatment in the past was to advise the patients to go home, rest and eat a nutritious diet.

Dr. E. Myles Standish, Hartford, Conn.: Patients with rosacea have been treated by dermatologists for years with hydrochloric acid, and many have shown improvement. In these instances, I suppose, the riboflavin was absorbed in the presence of the hydrochloric acid, and the improvement probably would not have occurred in the absence of hydrochloric acid.

Dr. Perry C. Baird Jr., Boston: How do you explain the occurrence of rosacea keratitis in only one eye?

Dr. Harold J. Jeghers (by invitation), Boston: I have seen a number of patients with rosacea keratitis in one eye, with the condition appearing later in

the other eye. Many show microscopic changes which can be seen only with the slit lamp. One is usually able to relieve the subjective condition of the eye in three or four days. Organic regression comes more slowly.

Cheilitis Exfoliativa. Presented by DR. FRANCIS P. MCCARTHY, Boston.

R. D., a 37 year old woman, has had scaling of the lips and elbows for about one and a half years.

She has white, scaling dermatitis on both lips with moderate dryness. Both elbows reveal fading psoriatic lesions.

She was given patch tests with samples of lipstick, tooth powder, nail polish and nail polish remover. All the reactions were negative. She was treated with nicotinic acid, 50 mg. three times a day, application of a proprietary tar ointment to the lips and of ethyl chloride to the elbows and ultraviolet irradiation of the lips, with no definite results.

DISCUSSION

DR. E. LAWRENCE OLIVER, Boston: I understand that cheilitis often responds to riboflavin, and since there is still ulceration of the mouth in this case, why not try riboflavin?

DR. BERNARD APPEL, Boston: I suggest a diagnosis of psoriasis for all the lesions, including those on the lips. I saw this patient on the date of her first visit to the outpatient department, and the scaling was much more evident than it is now. I suggested the application of a mild ointment containing salicylic acid, following which a large proportion of the patches disappeared. Subsequent to that I saw her again, at which time there was a slight recurrence, which in my opinion fits in fairly well with a diagnosis of psoriasis of the lips.

DR. JOHN G. DOWNING, Boston: I agree with Dr. Appel. The whole picture fits in with a diagnosis of psoriasis.

DR. FRANCIS P. MCCARTHY, Boston: In all cases of cheilitis with scaling of the lips or ulceration or commissural fissuring the condition is now immediately branded as a deficiency disease. I am amazed at the amount of nicotinic acid and other vitamin preparations being prescribed on the basis of the high pressure visits of the pharmaceutic agents. They have sold the medical profession the idea that scaling of the lips and fissuring of the angles of the mouth result from a deficiency condition. Vitamin deficiencies may be common in the south, and I am familiar with pellagra and beriberi, as I observed many cases of these diseases in Panama in 1908 and 1909. In the north, patients with typical pellagra are usually in the rural districts, and alcoholic addicts generally show the deficiency condition in the cities. A common cause of commissural fissuring is improper fitting of dentures causing tension at the angles of the lips. I suggest that the teeth be properly studied and a few other simple observations of the oral cavity be made before a definite diagnosis of vitamin deficiency is made. The term cheilosis is a misnomer, but cheilitis best fits the inflammatory picture and should be retained. If psoriasis of the skin can be determined by scratching the scale from a lesion and showing the presence of bleeding points from the increased vascularity of the papillae, why not test the lips in the same way? I am content to call the condition in this case exfoliative cheilitis with a question as to the cause.

Lichen Spinulosus. Presented by DR. WALTER GARFIELD, Boston.

E. B., a 37 year old woman, has had a moderately pruritic dermatosis on her back for several months. Although the patient appears to be well fed, her dietary intake is poor in fresh fruits, vegetables and milk.

There are many grouped follicular lesions on the back with a tendency toward grouping in small patches and spinous projections from the follicles.

She has received brewers' yeast, 2 teaspoonfuls twice daily for several weeks without any apparent benefit.

DISCUSSION

DR. JOSEPH GOODMAN, Boston: It might be worth while to investigate a case of this kind from the standpoint of vitamin A deficiency. The appearance of the follicular keratotic lesions is suggestive of that disease. In a number of instances of what I believe are lesions caused by vitamin A deficiency, I have seen this same configuration and the same distribution on the back. I suggest adding halibut liver oil to the diet.

DR. BERNARD APPEL, Boston: All the projections were definite thin plugs within the follicles. I examined one area carefully and pulled out a plug; it came out of a follicle and left a pinhole-like opening. From that I presume it was a follicular plug.

Dermatitis Medicamentosa. Presented by DR. J. H. SWARTZ, Boston.

M. C. S., a 53 year old woman, had numerous small intensely pruritic white lesions on the medial surfaces of the legs and knees which had developed one week prior to the first visit to the hospital. On the morning following the onset lesions appeared on the entire body and were bright red. She had been taking "Guyer pills" for abdominal pains every day for the preceding week. These contain "simple antacids" only, according to the formula on the package. Also, she had been taking "alophen" (aloin, extract of belladonna, powdered ipecac and phenolphthalein), but she was not sure whether she had taken any before the eruption developed. She gives no history of taking any other drug.

The skin of the cheeks showed numerous discrete small bright red macular and papular lesions, some of which showed fine vesiculation. The palms were free. The soles showed a few discrete macular lesions along the medial borders. The skin on the remaining portions of the body showed numerous discrete and confluent bright red macular, papular and small vesicular lesions. At present these lesions are violaceous, and many show fine scaling.

The white blood cell count was 4,950 per cubic millimeter. The blood smear showed 14 per cent eosinophils.

DISCUSSION

DR. E. LAWRENCE OLIVER, Boston: I think another diagnosis to be considered is pityriasis rosea. This eruption is widespread, and the long axes of the lesions seem to follow along the natural lines of the skin. The lesions are covered with scales, and there are no lesions on the face and scalp. I do not believe the condition is dermatitis medicamentosa.

DR. JOHN G. DOWNING, Boston: I agree with the diagnosis of pityriasis rosea.

DR. O. JOHNSON, Portland, Maine: Do you find macular lesions on the palms and soles in cases of pityriasis rosea?

DR. E. LAWRENCE OLIVER, Boston: It would be unusual. I do not recall that I have ever seen them, but in this case there is a possibility that the lesions on the palms and soles are pityriasis rosea.

DR. JOHN G. DOWNING, Boston: I have observed 2 cases of severe pityriasis rosea; in one there were papular lesions on the soles and palms and the condition lasted four months. Nine serologic tests for syphilis gave negative results. In the other case there were papular and vesicular lesions on the palms and soles.

DR. JOSEPH GOODMAN, Boston: I have seen a patient with pityriasis rosea with a typical eruption on the body and vesicular lesions on the palms.

DR. AUSTIN W. CHEEVER, Boston: I do not think the condition in this case is syphilis. I think the color of the lesions is too bright and the itching is much against that diagnosis. Some of the lesions are too small and also the scaling is not right for such a diagnosis.

Hemiatrophia Facialis. Presented by DR. FRANCIS P. MCCARTHY, Boston.

Since the age of 6 years, G. P., a 42 year old Negress, has had a flattening of the left cheek and the skin of the left side of the lower jaw extending to the neck. This condition has persisted and has grown more apparent with age.

There is considerable atrophy involving the lower part of the eye, the left cheek and the ramus of the jaw and extending to the neck with increased pigmentation. There is also some atrophy of the forehead, where there is pigmentation. The tongue shows deviation to the left with muscular atrophy of the left half.

The blood gave a positive Hinton reaction.

DISCUSSION

DR. FRANCIS P. MCCARTHY, Boston: The condition in this case, with the absence of subcutaneous fat and muscles in the cheek, is interesting. The atrophy of the tongue is essentially a congenital condition.

Xerostomia; Benign Papillomatosis of the Lip, Vestibule of the Mouth and Gingiva. Presented by DR. FRANCIS P. MCCARTHY, Boston.

H. G., a 68 year old white woman, who has worn artificial dentures since the age of 21, has had a dry mouth for the past year, and a papillomatous growth has developed. The growth involves the vestibule and gingival crest, is whitish and extends from the bicuspid to the cuspid; there is also an active lesion near the left lower molar. The mouth is dry, and there is some fissuring of the lip.

Cultures and smears of material taken from the lesion show the presence of monilias.

Rosaniline blue has been applied locally, and nicotinic acid was administered, 50 mg. five times daily.

Microscopic examination of a specimen taken from the lesion in the vestibule of the mouth shows acanthotic epithelial proliferation with well differentiated cells and papillary extensions of connective tissue. There is a cellular infiltration in the corium. There is no evidence of malignancy.

DISCUSSION

DR. FRANCIS P. MCCARTHY, Boston: The plates the patient had been wearing for about fifty years are most interesting and unusual. They are what are called "floaters." They "floated" around in the mouth and produced the papillomatosus of the lips. The monilias found in the lesion had nothing to do with the lesion itself. I feel that the treatment that would be most advisable is electrodesiccation (with the area under procaine hydrochloride anesthesia), piecemeal, until the total lesion has been removed.

Telangiectasia. Presented by DR. WILLIAM MACDONALD, Boston.

H. F. H., a 38 year old woman, has had an eruption on the legs, thighs and body for nine months. The condition started as an indefinite erythema and has increased in severity.

There is a telangiectatic eruption on both legs and to a somewhat lesser degree on the thighs. The eruption, while telangiectatic, appears to present in places primary pinpoint-like lesions.

Microscopic examination shows flattening of the rete pegs and probably a slight hyperkeratosis. There is no edema or cellular infiltrate. The subpapillary zone shows slight perivascular edema and infiltration of lymphocytes with occasional mononuclear cells. There is no evidence of pigment of any kind, no dilatation of capillaries or veins and no hemorrhages. The subcutaneous tissue shows slight fibrosis of the adipose tissue. There is atrophy of the sweat glands.

DISCUSSION

DR. JOHN G. DOWNING, Boston: I think the condition in this case is acrodermatitis atrophicans chronica.

DR. VINCENT RYAN, Providence, R. I.: This condition is an early stage of dermatitis atrophicans chronica.

A Case for Diagnosis (Necrobiosis Diabeticorum?). Presented by DR. FRANCIS P. MCCARTHY, Boston.

For the past one and a half years H. F., a 56 year old junk dealer, has had lesions on the backs of his hands and on the extensor surfaces of his legs which develop following trauma. Recently he has complained of neuritic pain in his right foot. He has diabetes, and he has partaken of ½ to 1 pint (250 to 500 cc.) of alcoholic liquor a day at the expense of an adequate dietary intake.

There are many depressed, atrophic, violaceous scars on his hands and legs. There is hyperesthesia of the hands, forearms, legs and feet to pinprick, cotton, heat and cold. The vibratory sensation is diminished over both ankles, especially the right.

He showed a fasting blood sugar of 165 mg. per hundred cubic centimeters. He received brewers' yeast in tablet form, 3 Gm. thrice daily.

DISCUSSION

DR. FRANCIS P. MCCARTHY, Boston: This patient was seen in consultation with members of the medical service because bullous lesions were developing following trauma. A diagnosis of pemphigus had been made. One was able to reproduce lesions on the backs of the hands by slight trauma. There were numerous scars present on the legs with one scaly lesion on the right shin. Dermatologists certainly have gone off on a tangent by blaming vitamin deficiencies for any obscure dermatitis. It is interesting to notice the bullous lesion on the patient's hand today, which was produced by slight trauma.

DR. WALTER GARFIELD, Boston: He also has a history of being an alcoholic addict but stated that he ate well.

DR. J. HARPER BLAISDELL, Boston: This brings to mind that in the olden days people had their vitamins and alcohol combined in the form of hot buttered rum, egg nogs and rum fruit punches.

DR. BERNARD APPEL, Boston: I do not see anything inconsistent in these lesions with a diagnosis of erythema multiforme bullosum. Bullous lesions come and go on the backs of the hands and on the legs and leave pink scars.

DR. FRANCIS P. MCCARTHY, Boston: The difference between this patient's condition and erythema multiforme bullosum is that this condition is a spontaneous eruption produced by trauma.

DR. E. LAWRENCE OLIVER, Boston: I suggest a diagnosis of epidermolysis bullosa aquisita. I think there is such a disease. The appearance of the lesions after slight trauma is in favor of this diagnosis. I do not believe the condition is pemphigus.

Lymphangioma Circumscriptum. Presented by DR. WILLIAM B. COHEN, Providence, R. I.

B. D., a 12 year old girl, has had an eruption on the thigh for nine years. The eruption is spreading.

Examination shows an ill defined papular eruption of closely grouped lesions on the medial surface of the right thigh. Microscopic examination of the tissue showed a layer of stratified epithelial cells that had brown pigment in its basal layer. Below this there was much collagenous tissue, the base of a hair follicle, sweat glands and fat. There were a few lymphocytes scattered in the tissue. The corium seemed much denser, with increased hyalin, and contained several dilated lymphatic spaces.

DISCUSSION

DR. E. LAWRENCE OLIVER, Boston: The condition seems to me to be a typical example, clinically, of lymphangioma circumscriptum. The lesions are deep-seated vesicles, and some show slight hemorrhage. The eruption has existed since the patient was a child, and it has spread slowly, which is characteristic of this condition. I think treatment with roentgen rays, or with radium would clear it up fairly rapidly. Often the lesions in a case of this kind are not present at birth but appear during childhood or, occasionally, not until adult life.

DR. FRANCIS P. MCCARTHY, Boston: The microscopic examination confirms the clinical diagnosis. There are dilated lymph vessels which are located superficially just below the epithelial layer.

DR. JOHN G. DOWNING, Boston: The treatment indicated is excision. In this location excision could be easily done.

DR. E. MYLES STANDISH, Hartford, Conn.: I would be more in favor of electrodesiccation. There would probably be very little scarring, and this would be better from a cosmetic standpoint.

PHILADELPHIA DERMATOLOGICAL SOCIETY

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Jan. 17, 1941

Erythema Chronicum Migrans (Lipschütz). Presented by DR. PATRICIA DRANT.

L. O., a white woman aged 52, was presented before this society last year (ARCH. DERMAT. & SYPH. **42**:746 [Oct.] 1940). She has an eruption which began on the dorsum of the right hand four years ago as erythematous papules. The infiltrated erythematous margins spread peripherally, with coalescence of the lesions and development of slight atrophy in the centers. For three years the eruption was limited to the dorsum of the right hand and to the extensor surface of the right forearm. The same surfaces of the left hand and forearm became involved one year ago, and the upper thoracic region six months ago. Lesions are beginning to appear on the exposed "V" of the neck. There are no subjective symptoms. Serologic tests of the blood for syphilis gave negative results.

DISCUSSION

DR. PATRICIA DRANT: My first diagnostic consideration in this case was granuloma annulare, but the lesions did not seem typical of that condition. There was not enough infiltration; the dermatosis was extensive, and there was considerable erythema of the margins. At the first presentation no diagnosis was made.

DR. J. V. KLAUDER: I do not regard this condition as erythema chronicum migrans of Lipschütz. My concept of the latter disease is that it starts from a localized area, such as the bite of an insect, and then extends peripherally, forming a large ring; it may extend over a large portion of the trunk in a wavelike manner, with sharply marginated, slightly elevated, erythematous borders. I am interested in this type of lesion from the standpoint of comparative studies of the lesion—the wavelike erythema is similar to that occurring in generalized erysipeloid of Rosenbach (Klauder, J. V.: Generalisiertes Erysipeloid: bericht über einen 29 Monate dauernden Fall mit Sektionsbefund, *Dermat. Wchnschr.* **98**:613, 1934).

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I recently saw a woman who was stung by an insect in the left scapular region. This produced an inflammatory reaction, with subsequent healing. However, at this site an almond-sized area of marginated erythema periodically develops, which is very itchy. In this particular case there is no migratory phenomenon but a recurrent annular erythema. I believe the case presented is one of granuloma annulare. The lesions are non-inflammatory; the centers are clear, and the margins are yellowish brown and on palpation feel firm and indurated.

DR. HERMAN BEERMAN: There are certain features that suggest lichen planus, particularly the oral lesions.

DR. FRED D. WEIDMAN: As I recall from the previous presentation, there was general agreement that the centers of the patches were atrophic and, to my mind, in a way that is never seen in lichen planus. Of course, atrophic lichen planus is seen, but not the smooth, shiny-surfaced skin with blood vessels shining through that is noted here. I think at the previous presentation I raised the question as to the possibility of porokeratosis of Mibelli. I do not know what the correct diagnosis is clinically, but I have a definite idea about the biologic features after seeing the sections. There are a round cell infiltration with nodular infiltration around the blood vessels, much denser than that seen in ordinary diffuse inflammation of the skin, and thickening of the blood vessel walls. A particularly striking feature is the presence of foreign body giant cells around certain fragmented collagen bundles, entirely apart from the lymphocytes. I sense that there is a degeneration of collagen due to a vascular disturbance which can result in necrobiosis. This woman has a striking vasomotor instability, and as a result of spasm of the blood vessels there might be shutting off of nutrition of the collagen bundles with a resultant foreign body reaction. The annular configuration may be referable to the distribution of some particular arterial system of the skin. It may finally be decided clinically that this condition is the chronic migratory erythema of Lipschütz, and that might throw some light on the pathologic nature of that condition. I read the short paragraph on this disease in the textbook of Sutton and Sutton, but, as I interpreted it, in that entity the erythema is uniform and diffuse in type, while in this case it is nodular. On the back of the patient's neck there is a tiny ring, not more than 0.5 cm. in diameter, which shows no erythema; it is altogether colorless, just as I should expect after seeing the microscopic foci of dead collagenous tissue in the section. This mechanism is similar to granuloma annulare, so far as the basal pathologic processes are concerned; but I should say definitely that the subsequent course, the extent to which atrophy takes place and, for that matter, the general histologic picture are definitely not those of granuloma annulare.

DR. MARION B. SULZBERGER (by invitation), New York: I have no absolute opinion as to the diagnosis, but I think that the condition is probably not erythema chronicum migrans of Lipschütz, according to the descriptions I have read and the typical cases I have encountered. Erythema chronicum migrans is much more acutely red and inflammatory, and not infiltrative, as the lesions in this case seem to be, both clinically and histologically. I believe that if I were forced to label this condition I should be in favor of calling it an atypical granuloma annulare, particularly since Dr. Weidman has just said that the histologic picture is at least similar to that seen in granuloma annulare. I think there are many atypical forms of granuloma annulare, just as there are of other diseases, and some cases of these atypical forms which have been described present a picture closely resembling that in this case, both histologically and clinically.

Calcinosis with Scleroderma. Presented by DR. PATRICIA DRANT.

V. H., a white woman aged 65, a spinster, was apparently well until Feb. 23, 1927, when an attack of urticaria suddenly developed which was severe enough to require admission to a hospital. This subsided promptly, but shortly thereafter

the patient suffered an attack of tonsillitis and bronchitis, with development of arthritis of the right knee. These conditions subsided, and the patient remained apparently well until December 1937, when swelling of the hands, knees and face was noted. Cutaneous tests for allergy showed a polyvalent sensitivity. Three teeth with apical abscesses, demonstrated by roentgenograms, were extracted. Culture of material from the abscesses showed pure hemolytic streptococcus.

In April 1938 a dermatitis developed on the wrist under her watch and on the outer aspects of the knees and elbows. This gradually extended until the entire cutaneous surface was involved, by July. The patient was first seen by the presenter in October and was suffering from an extensive exfoliative dermatitis associated with severe pruritus. Bacterial cultures of material from the upper respiratory tract revealed Streptococcus haemolyticus. There was a remission of the dermatitis after the administration of an autogenous vaccine. An ointment containing 8 per cent viosterol in an oxycholesterol-petrolatum (aquaphor) base was the most effective topical treatment. The administration of sulfanilamide caused asthenia and an exacerbation of the dermatitis and pruritus. In August 1939 the patient had bronchopneumonia and was given sulfanilamide. The skin showed improvement. Enlargement and irregularity of the liver were noted for about six months. This condition became acute, and a cholecystectomy was performed. Again there was a remission of the dermatitis. In February 1940 a calcareous nodule was first noted in the left scapular region. Subsequently large deposits of calcium were laid down in dependent portions of the skin, namely, the tip of the chin, the elbows, the buttocks, the inner aspects of the thighs and the knees. Roentgenograms showed the typical lacy distribution of calcium in the skin and subcutaneous tissue. The distal phalanges of the fingers showed the diagnostic absorption with pointing of scleroderma.

DISCUSSION

DR. REUBEN FRIEDMAN: My patient with calcinosis differed from this one in that she did not have the exfoliative dermatitis that this patient presents and that nothing seemed to have any influence on the course of the condition other than some estrogenic substance, and that influence was questionable.

DR. FRED D. WEIDMAN: One should always remember the difference between calcinosis and calcification in scleroderma. The latter is a simple regressive process not tied up with parathyroid metabolism or any other endocrine factors, so far as is known. This patient has a dense skin. I can understand how one would call the disease scleroderma when the skin at the side of the face is palpated. It is certainly bound down—much more firmly than it is in ordinary generalized erythroderma, for example. I do not think that the condition in this case is a classic example of scleroderma, but there is a good deal more fibrosis in the deeper parts of the skin than is commonly seen in an ordinary generalized exfoliative dermatitis. Was the viosterol administered only locally? Was it not given by mouth?

DR. PATRICIA DRANT: Two years ago she was given viosterol by mouth.

DR. FRED D. WEIDMAN: All physicians are aware of the hypercalcemia which can be induced by extensive vitamin D medication.

DR. PATRICIA DRANT: But I have found nothing in the literature about hypercalcemia developing after such an interval. In the last six weeks the patient has had extreme asthenia.

DR. FRED D. WEIDMAN: I wonder whether this patient has had a generalized dermatomyositis and whether in the fibrous tissue there is a development of calcification without a real calcinosis. True, the deposits in calcification do not occur in this isolated plaquelike form; that form is typical for calcinosis. I should wish to consider this case at length before saying definitely that the condition is not a calcinosis.

DR. ROBERT L. GILMAN: I think the concept of the case depends on the history. Dr. Drant wisely stated that in exhaustive studies no cause has been found and that probably the nearest approach to the cause was gallbladder disease, which might have produced a disturbed metabolism of fats. I suggest the administration of small doses of solution of parathyroid in an effort to reroute the calcium. It might be interesting to determine in what form the calcium is deposited.

DR. FRED D. WEIDMAN: The history of repeated attacks of severe acute infections suggests the possibility of scleredema adultorum (Buschke) as an explanation of the subcutaneous thickening.

DR. MARION B. SULZBERGER (by invitation), New York: I am inclined to agree that the underlying cause in this case is a recurrent infectious process which has affected many systems, including, perhaps, the calcium-regulating system. It seemed to me that in the roentgenograms the pelvis showed some evidence of osteoporosis.

Erythema Multiforme Bullosum. Presented by DR. PATRICIA DRANT.

A. G., a Negress aged 12 years, presents a generalized bullous eruption, including the mucous membranes of the mouth and tongue. The child has had "asthma" since infancy and has had a bullous eruption of varying severity for four years, usually after excessive intake of sugar. Fish, eggs and milk produce gastric distress. The patient drinks large quantities of water. Tests for sugar tolerance gave normal results. Cultures of the blood and of material from the lesions were sterile. The nonprotein nitrogen, uric acid and creatinine levels of the blood were normal. Repeated urinalyses showed slight reactions for albumin, faint traces of sugar and an occasional hyaline cast. The Wassermann reaction of the blood was negative. Cutaneous tests for allergy with eggs, fish and milk also gave negative results. Nikolsky's sign can be elicited. A patch test with 25 per cent potassium bromide in petrolatum caused a strongly positive reaction.

DISCUSSION

DR. J. V. KLAUDER: I do not believe that this condition is erythema multiforme bullosum, for the bullae appear at points of pressure and not in the center of the patches of erythema. I think the patient has epidermolysis bullosa.

DR. CARROLL S. WRIGHT: The possible diagnoses of bullous eruptions are limited. Aside from erythema multiforme bullosum, dermatitis herpetiformis, pemphigus, epidermolysis bullosa and possibly drug eruption, there is not much one would have to consider in this case. I have not seen true pemphigus in a child. I do not agree with the diagnosis of erythema multiforme bullosum. I suggest a diagnosis of dermatitis herpetiformis, of which I have seen 2 or 3 examples in children. I have observed a good response to arsenic in the form of solution of potassium arsenite U. S. P. I think this treatment might be worth trying here.

DR. J. V. KLAUDER: I think it would be desirable to examine the conjunctivas of this child to see if there is a process analogous to ocular pemphigus. That process occurs with some bullous eruptions other than pemphigus. I recall, for example, the report of such a condition by Sulzberger and Cohen (Cohen, M., and Sulzberger, M.: Essential Shrinkage of Conjunctiva in a Case of Epidermolysis Bullosa Dystrophica, *Arch. Ophth.* **13**:374 [March] 1935).

DR. MARJORY HARDY: I examined the child's conjunctivas and found nothing abnormal.

DR. LOUIS GOLDSTEIN: I saw a few lesions undergoing involution that were typical of erythema multiforme.

DR. FRED D. WEIDMAN: I examined closely the points of pressure and did not note that the bullae were particularly localized to these sites—in fact, they were

free of lesions. The patient states that her skin itches. There are scars on the shoulders. Although the dermatitis is remarkably symmetric for dermatitis herpetiformis, I think that disease has to be considered, possibly the type known as hydroa puerorum.

DR. PATRICIA DRANT: On a highly restricted diet and with massive doses of vitamin D, every lesion on this child's cutaneous and buccal surfaces disappeared. I was able to produce this outbreak by administering a half-pound (225 Gm.) of chocolate candy, to which there was an immediate response.

A Case for Diagnosis (Dermatitis Factitia?). Presented by DR. J. V. KLAUDER.

E. H., a white man aged 43, well nourished and well developed, was first seen in April 1940. At that time he had scattered superficial ulcers and scars on the lower part of the abdomen, the thighs and the scrotum of two months' duration. The ulcers were sharply marginated and varied from 3 to 5 cm. in diameter. They disappeared and recurred. Through repeated examinations it was observed that at times some of the ulcers had a tail-like area of erythema. There was no odor about the new lesions. The patient states that new lesions appear suddenly at 2:30 a. m.; at this time he experiences a burning sensation which awakens him. The ulcerations cause partial incapacitation, but he appears anxious to continue his work and refuses admittance to the hospital. The results of physical examination are essentially normal. The corneal reflex is partially abolished; the laryngeal reflex is present. The Wassermann reaction of the blood was negative. The blood sugar amounted to 98 mg. per hundred cubic centimeters. On one bacteriologic examination, Bacillus coli was found. This organism was not obtained on repeated subsequent examinations. The biopsy specimen showed a picture of nondescript nature. The patient has been subjected to psychiatric examination, with no significant results.

DISCUSSION

DR. CARROLL S. WRIGHT: This man came to my clinic recently. A great many of the lesions were weeping and exuding, particularly those on the lower part of the abdomen. I presented him to a group of students with the remark that I was unable to make any definite diagnosis and suggested the possibility that the condition might be self induced, particularly in view of the fact that a number of the lesions were linear and bizarre. Recently a specimen of a new lesion on the back of the neck was taken for biopsy. Blood was taken for serologic tests and for cultures, both of which gave negative results. In view of the fact that there was a certain amount of infection present, I gave the patient sulfanilamide in full therapeutic doses by mouth. A lotion containing 2 grains (0.13 Gm.) of mercury bichloride to 6 ounces (180 cc.) of calamine lotion was prescribed, and today the lesions are practically dry. Frankly, I cannot fit this condition into any clinical entity. The man gives no history of having taken drugs. I still feel that the most probable diagnosis is dermatitis factitia.

DR. J. V. KLAUDER: I came to the conclusion that the condition was dermatitis factitia after some time. The other members of the staff thought it was dermatitis factitia months before I admitted it. I agreed with them at the time that I saw a linear band of erythema attached to one of his superficial ulcerations, which the English call a "telltale trickle tail," produced by the application of caustic. Saponated solution of cresol is usually employed in such cases, but I never could detect any odor of it. Psychiatric examination was not of any help. I believe that the psychiatrist missed the point. He reported "No psychosis." If he had said "There is no evidence of hysteria," I think that would have been correct. The man was anxious to work, but that is characteristic of all patients with this condition. Perhaps he realized that the eruption was suspected of being self produced and asked to be transferred to another clinic.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I think the patient has a "telltale" lesion in his left groin; it is linear and has the grayish purple color seen after application of a phenol preparation.

DR. J. V. KLAUDER: At one time gentian violet (a form of methylrosaniline) was prescribed; perhaps he applied it recently.

DR. LOUIS GOLDSTEIN: Would it not be a simple matter to have one limb bandaged and observe the patient for a while?

DR. J. V. KLAUDER: I wanted to do that, but the patient continuously refused to be admitted to the hospital. I wished to carry out another helpful means of diagnosis, namely, to say in his presence that I thought a certain area of skin looked as if a new lesion were going to appear. If a new lesion had appeared subsequently at the indicated site, that would have been additional evidence of dermatitis factitia.

DR. FRED D. WEIDMAN: My first thought was dermatitis factitia, but when I came to examine the composition and texture of the lesion I felt some reservations about that diagnosis. The more elevated lesion has a translucent quality, an apple jelly effect, that I cannot conceive as the result of anything applied locally, with production of so much hyperplasia of tissue, unless that lesion is an early beginning keloid. That may be the case. In lymphangioma circumscriptum one sees linear lesions not uncommonly, and the patient states that at times the lesions ooze. I punctured one of these clearer elevations and was a little disappointed to find that it did not trickle. The skin of his scrotum at the most dependent part is much thicker than is normal, and that is a site where lymphangioma circumscriptum occurs when the lower part of the abdomen is involved. The lesions on the back show a gradual fading out, which I think is more in line with spontaneously developing lesions than factitial ones.

DR. H. E. TWINING: The interesting point is that this man can tell the exact minute that he has an outbreak. These lesions are new; the old ones have healed. In possibly another week or two the skin will be almost clear, and then a week later new lesions will occur. By the time the patient is able to go to work, a new crop of lesions will appear.

DR. J. V. KLAUDER: I wanted to give this patient sodium amytal intravenously, as reported by Eaton and O'Leary (ARCH. DERMAT. & SYPH. **36**:544 [Sept.] 1937) and then ask him while under anesthesia what he is using to produce the lesions. Perhaps Dr. Wright may induce a psychiatrist to do this.

DR. FRED D. WEIDMAN: Has any one in this room ever used the confrontation test successfully?

DR. J. V. KLAUDER: I had a private patient, a young girl, whom I strongly suspected of using saponated solution of cresol to produce cutaneous lesions. I told the nurse to search her room for a bottle of this solution, and she found it under the patient's pillow. When questioned, the patient explained it very cleverly and in a way that helped me in telling her husband the correct diagnosis. She said that her family doctor had told her that her condition was a streptococcic infection—as he had—and she was using the saponated solution of cresol as an antiseptic! About three years later a surgeon communicated with me to the effect that this patient was then under his care and was anxious for an operation. He was not certain that such an operation was necessary.

DR. ROBERT L. GILMAN: I think that when one talks to a patient, for instance, one with excoriated acne, and the patient admits, on cross questioning, that he is producing the lesions, one will get a confirmation of what is known to be the fact, that the patient rationalizes the procedure so well that it takes away most malingering elements. I have found that patients with acne who scratch themselves do it subconsciously or with a rationalization.

DR. HERMAN BEERMAN: Other dermatologists who have seen patients with dermatitis factitia have found that as soon as the patients are informed that their methods are known they promptly cease to come for treatment. Some patients when confronted become indignant. In one case the husband even threatened to sue the physician for slandering his wife.

Acute Lupus Erythematosus Disseminatus. Presented by DR. H. E. TWINING.

M. W., a white woman aged 48, presents an erythematous, confluent, edematous area, varying from bright red to a dusky appearance, with a certain degree of vesiculation and exudation in some areas. At present the skin has a dusky hue, fine scales and in certain areas atrophy. The temperature varies from 99 to 103 F. She has general malaise and weakness and complains of pain and tenderness in the involved areas. The patient has always enjoyed excellent health until about nine months ago, when an erythematous area developed on the back and shoulders. This was treated for two months with roentgen rays, and then there was a rapid spread, the condition involving the entire upper portion of the body to the waistline with itching, burning and tenderness. Physical examination revealed no abnormal condition except on the skin. The patient has lost about 20 pounds (9 Kg.). Urinalysis showed a slight reaction for albumin. Examination of the blood revealed decided leukopenia. The patient was given injections of whole blood, quinine, a bismuth compound, sulfanilamide and finally ultraviolet irradiation of the blood, with definite improvement.

DISCUSSION

DR. H. E. TWINING: The treatment which has given the best results in this case is the reinjection of the patient's blood after irradiation with ultraviolet rays. The blood is withdrawn, exposed to water-cooled ultraviolet radiation and then reinjected into the blood stream. The method was devised by E. K. Knott, of Seattle. A needle is inserted into the vein and kept there, and I believe about a pint (475 cc.) of blood is drawn into the chamber, which is partially covered. It is really a wheel with quartz windows in it. The blood is exposed to off and on irradiation for possibly fifteen to twenty minutes and then is reinjected into the vein. I thought this patient was going to die and had employed practically all methods of treatment, including sulfanilamide. More or less in desperation, I subjected the blood to mild treatment, about half a dose (two and one-half seconds for each 5 cc. of blood) and on that day the temperature returned to normal and has remained so. The lesions have been gradually disappearing, but the patient is still far from well. Whether she is going to have any relapses I do not know. If there are any suggestions for further treatment, I should like to receive them. About three weeks ago I administered 10 mg. of gold sodium thiosulfate, but I thought a slight exacerbation occurred and discontinued its administration. At present the irradiations are given about once a month, and in the meantime I am administering a bismuth compound intramuscularly. I should like to know whether any one thinks that treatment with a gold compound is indicated in this type of case or not.

DR. J. V. KLAUDER: I saw the patient on one occasion. At this time she presented a dusky erythema of the face and upper part of the trunk. Although she had a fever and had lost some weight, she did not appear to be as acutely ill and prostrated as one would expect with acute lupus erythematosus disseminatus. Various forms of treatment were employed; so it is difficult to reach a conclusion as to the role that ultraviolet irradiation of the blood played in the improvement.

DR. CARROLL S. WRIGHT: In 1928 a patient was brought here from Tennessee to see Dr. Schamberg. She had a temperature of 103 F., and I wondered how the physician in charge of the patient dared to move her in that condition. She presented a lupus erythematosus of the face on which some form of caustic treat-

ment had been used, with the development of a high temperature. Dr. Schamberg then started to expose the whole body, except for the affected areas, to ultraviolet radiation every day, and—much to my surprise—in about two weeks the temperature became normal. During this time she was constantly confined to bed. Later the patient was able to take a gold compound in gradually increasing doses and made a complete recovery. Three or four years ago she was well. The condition in this case was not strictly a disseminated type but an acute flare-up of a chronic type. I think, therefore, that a gold preparation might be tried cautiously in Dr. Twining's case.

Hidradenitis Suppurativa, Papulonecrotic Tuberculid and Bromoderma. Presented by Dr. John B. Ludy and Dr. Patricia Drant.

T. L., a Negress aged 29, presents suppurative sinuses in the axillas and in the inguinal region and also a bromide eruption. She has had intermittent infection of the axillas for seven years. The inguinal infection is of one year's duration. She has been taking bromides since September 1940. The blood sugar content was 104 mg. per hundred cubic centimeters, the blood urea 9 mg. and the blood bromide 40 mg. An anaerobic streptococcus was recovered from pus from the axillary lesions. The reaction to a Frei test was negative. The protein content of the serum was 7.8 Gm. per hundred cubic centimeters. A blood count was normal. Repeated Kahn tests gave negative results. A blood culture showed no growth. The urine was normal.

DISCUSSION

Dr. J. M. Schildkraut, Trenton, N. J.: The condition in the axilla suggested clinically a scrofuloderma.

Dr. Fred D. Weidman: At a meeting of the Chicago Dermatological Society (Arch. Dermat. & Syph. **43**:1143 [Dec.] 1940), Dr. O'Leary cited a surprisingly large number of cases of this kind. I recall that the condition is not confined to the axillas but may occur in other parts of the body. He mentioned the scalp, citing the fact that there are such structures as apocrine glands in the scalp. I wonder whether these nodules might not possibly be disseminated lesions of the same condition. The practical point in treatment cited by O'Leary is that the only successful method is surgical excision.

Dr. Marion B. Sulzberger (by invitation), New York: I think that hidradenitis is relatively common; of course, the ordinary form is in the axillas. This condition used to be diagnosed simply as "boils" of the axillas. The same process can occur in any situation in which there are apocrine glands, and these glands can be well scattered over the body, particularly in the pubic region, the perianal and perivulvar areas and along the mammary ridges. It would, however, be unusual to see such glands scattered over the extensor surfaces of the arms. I do not agree that surgical excision is necessary for ordinary hidradenitis axillaris. In an ordinary case the condition often does well with roentgen rays, hot wet dressings and proper hygienic care of the axillas. I think that some of the causative factors of hidradenitis are highly interesting. I have encountered cases in which there was no doubt that the hidradenitis followed an axillary dermatitis, for example, from dress shields, deodorants, depilatories or dress dyes. In one the causal factor was not an external irritant but injection of androgen. A man who was receiving androgen for eunuchoidism had hidradenitis of the axillas every time he received an injection. One can see the same effect of androgen in other glands of the skin, namely, in the related sebaceous glands and in the production of lesions of acne.

Gumma of the Tongue. Presented by Dr. John B. Ludy and Dr. Patricia Drant.

R. P., a Negro aged 36, presents an irregular, infiltrated mass involving the anterior surface of the tongue. The lesion is tender and has bled occasionally, and

there is an extensive regional adenopathy. The patient had a mass at the base of the tongue in November 1939, six weeks after a tonsillectomy. A biopsy specimen from this lesion showed chronic inflammatory tissue, and culture revealed hemolytic staphylococci, Vincent's spirillums and fusiform bacilli. At that time the lesion regressed after the administration of sulfanilamide and topical application of various silver compounds. The biopsy specimen from the mass showed chronic inflammatory tissue. The Wassermann and Kahn tests of the blood gave a 2 plus and a 1 plus reaction, respectively. Inoculation of a guinea pig with tissue from the tongue produced no evidence of tuberculosis in two months, and a culture for fungi showed no growth.

DISCUSSION

DR. J. V. KLAUDER: This lesion does not impress me as a gumma. It does not infiltrate the tongue, as would be expected if it were a late lesion of syphilis. It impressed me as a growth arising from the surface of the tongue.

DR. FRED D. WEIDMAN: The lesion suddenly and abruptly projects above the general level of the skin, as Dr. Klauder said; it is a fungating lesion. It is translucent, and the texture is uniform throughout. I do not think that translucency would be observed in a tertiary syphilitic lesion, and a tertiary syphilitic lesion of that size should have ulcerated by this time. The lymph nodes are huge. The possibility of lymphangioma was suggested by one of the graduate students; the lymphadenopathy in the neck is, I think, rather against that diagnosis. I examined a portion of tissue (by teasing), which was sent to the laboratory for culture and stained under the cover slip. It consisted solely of epithelial cells; there was not a trace of inflammatory infiltrate in the seven or eight particles I examined. My impression was that the condition might turn out to be a cornifying squamous cell cancer.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I suggest a therapeutic test to rule out syphilis.

NOTE.—The patient showed definite improvement following antisyphilitic therapy.

NEW YORK DERMATOLOGICAL SOCIETY

EDWARD R. MALONEY, M.D., *President*

J. GARDNER HOPKINS, M.D., *Secretary*

Jan. 28, 1941

A Case for Diagnosis (Radiodermatitis? Dermatitis Factitia?). Presented by DR. EUGENE F. TRAUB.

L. K., a woman aged 20, entered the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital six or eight weeks ago with open ulcerations of the fingers and sloughing of the nails. Since then the ulcerations have healed under treatment with boric acid ointment.

At the time she first visited the clinic the majority of the physicians who saw her thought the ulcerations represented dermatitis artefacta rather than radiodermatitis, because of the peculiar way the patient claimed that she had held her hand under the x-ray tube, together with the way lead screening had been placed over the back of the hand. However, after further questioning it was learned that for the first three roentgen ray treatments the fingers, held upright, were placed in a cone with the first finger left out, the second, third and fourth fingers being fully exposed and the fifth receiving only a slight dose. At the time of the

fourth treatment the hand was laid flat, only the dorsal surface receiving the exposure (as the patient had originally described). Therefore, the reason for thinking of dermatitis artefacta rather than of radiodermatitis—because destruction followed not only on the dorsal but on the palmar surface—was no longer valid.

These treatments were given in September 1940, supposedly for a fungous infection of the nails. All four treatments were given by the same radiologist, three with one machine and the last, with the hand in a different position, with a different machine. After the last treatment the patient noticed a severe "burn" with blisters involving all of the fingers (undoubtedly caused by the first three treatments, judging from the position in which the fingers had been held). These lesions gradually improved except on two fingers, where the sequelae are still pronounced.

The patient is presented today for two reasons: first, to confirm the diagnosis of radiodermatis as against dermatitis artefacta; and second, if the condition is radiodermatitis, to find out what can be done about it. At no time during the original treatments was the patient seen by a dermatologist.

DISCUSSION

DR. GEORGE MILLER MACKEE: Two fingers showed atrophy and sclerosis of the skin and of the deeper tissues and slight telangiectasia. This, with the history, is presumptive evidence for chronic radiodermatitis, and that is presumably the correct diagnosis, but I do not feel like making a diagnosis unequivocally on one inspection. I can conceive of loss of nails, sclerosis and even this slight telangiectasia as resulting from other causes, combined with long-continued inflammation, and as a result of therapy.

DR. HOWARD FOX: It seems to me that the condition and the history of roentgen ray treatment fit in satisfactorily with a diagnosis of radiodermatitis.

DR. EUGENE F. TRAUB: Apparently no one thinks the condition is an artefact, which was the only other diagnosis considered. I believe the history of roentgen ray treatments given in the peculiar way they were given to this patient, together with the prompt healing with boric acid ointment and the course of events since I first saw her, makes the diagnosis reasonably certain.

A Case for Diagnosis (Lupus Erythematosus Disseminatus?). Presented by DR. FRED WISE.

A. G., a woman aged 39, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Jan. 23, 1941, with an eruption of six months' duration. In May 1940 both ovaries, which were cystic, and the appendix were removed. During the following three months she exposed herself to the sun for four hours daily. The skin did not tan but became red and itchy. The eruption appeared first in the middle of the extensor surfaces of the forearms and on the chest in a region corresponding to the entire area exposed by a V neck dress. Two weeks later the entire face became affected. She became weak and was confined to the house during September and October. On October 30 and November 15 the patient had two treatments with high voltage roentgen rays to the hypogastric areas. Within the following two weeks the eruption spread to the back, thighs, epigastric region and legs. She was treated during November and December with intravenous injections of calcium gluconate and administration of capsules of a preparation of liver and stomach extracts with iron (lextron). Her general condition improved, but there was no change in the rash. She complains of a feeling of heat in the body and of severe itching in the pelvic and inguinal regions. Her general health lately has been fairly good. She has lost 3 pounds (1.4 Kg.) during the last three months.

The patient is about 5 feet 4 inches (163 cm.) in height and weighs 118 pounds (53.5 Kg.). She presents a fairly symmetric patchy, generalized, dry, scaly erup-

tion involving the entire face, which is moderately edematous, and the neck, trunk and extremities. The patches are marginated and flat. Some patches, including those on the abdomen, are superficial, light red and level with the surrounding surface; others, such as those on the extensor surfaces of the legs, are purplish red and moderately infiltrated, with the surface rough and uneven with numerous scratch marks. In the patches located on the volar surfaces of the arms are numerous vesicular and bullous lesions which are fairly firm and have clear contents. The lesions on the lower extremities show on diascopic pressure generalized hemorrhagic puncta. The patient's temperature ranges from 99.5 to 100.2 F., rectally. The pharyngeal reflex is absent. There is a rough systolic murmur in the mitral area. Bean-sized soft glands are felt in both axillary regions. The hemogram was normal except for 9 per cent eosinophils and a platelet count of 200,000. The Wassermann and Kahn reactions of the blood were negative, and the icterus index and the results of chemical examination of the blood, including determination of cholesterol, were normal except for 2.9 per cent albumin (normal 4 to 5 per cent) and 2.4 per cent globulin (normal 2 to 3 per cent), with a ratio of 1:2 instead of the normal ratio of 1:6 to 2:1. The sedimentation rate was 30 mm. per hour (normal for females, 15 mm. per hour). The result of a capillary resistance test was normal.

Examination of the thorax showed a relatively small, elongated, dropped type heart. There are a moderate hilar thickening and generalized vascularity.

Histologic examination of a section of one of the isolated lesions on the forearm, examined by Dr. Satenstein and by Dr. Sachs, was reported as showing "bullous toxic dermatitis."

DISCUSSION

DR. GEORGE C. ANDREWS: I gained the impression, since the histologic picture was not that of lupus erythematosus, that this case might be one of dermatomyositis. The woman's history, the condition starting with a great deal of puffiness and swelling of the face and tenderness and weakness of alternate groups of muscles, indicates dermatomyositis. In some cases it is almost impossible to differentiate between dermatomyositis and lupus erythematosus of the acute generalized type. I suggest that, in addition to the laboratory examinations already made, a section of muscle be examined for hyaline degeneration and that the blood and urinary creatinine be determined.

DR. A. BENSON CANNON: I hesitate to make a diagnosis of acute lupus erythematosus in this case, although I am unable to offer a better one. I believe that the patient is in too good a state of general health to have such an extensive eruption of lupus erythematosus. So far as one can determine, she has no constitutional symptoms, and if it were not for the presence of the eruption she would be normal. The patient states that the outbreak on her skin appeared after she had taken a tonic for several months, and it was her impression that the tonic caused the condition I think that the eruption appears to be strikingly like one that follows the intake of one of the barbituric acid compounds.

DR. J. GARDNER HOPKINS: The areas where the eruption first appeared suggest that hypersensitivity to light is a factor, although I do not believe it is the whole cause. She has the eruption in the intergluteal folds and between the buttocks, and I thought she had real atrophy and telangiectasia on the knees. The tongue showed a little smoothness along the edge, but the papillae were not lost in the center. I am inclined to think the condition should be classified in the pellagra group of diseases, as due not to a pure nicotinic acid deficiency but probably to a multiple deficiency.

DR. EUGENE F. TRAUB: The question has been raised of the patient's being too ill for acute lupus erythematosus. One cannot generalize about this entity in this manner, because the condition of these patients can change rapidly. Symptoms not present one day may appear on the next. I presented a patient before this

society about four years ago as one with acute disseminated lupus erythematosus (ARCH. DERMAT. & SYPH. **36**:1302 [Dec.] 1937), a diagnosis with which the members did not unanimously agree because they thought the patient was in too good condition. The patient was dead, however, before the next monthly meeting, presenting a striking example of how rapidly this process can develop. I have another patient in the hospital now; ten days ago there was no heart murmur, but now there is. A vegetative endocarditis is apparently developing, and the medical consultant gives a prognosis of six weeks of life. Therefore, all the features of this disease do not have to be present at a given time.

DR. PAUL E. BECHET: In view of the atypical character of the clinical evidence, one cannot be dogmatic about making the diagnosis of a disseminate type of lupus erythematosus. The absence of any constitutional symptoms, however, does not exclude the diagnosis, as it is a well known fact that an acute typical extensive disseminate lupus erythematosus frequently occurs without in the least affecting the patient's general health. It is now also well known that light sensitivity may occasionally prove to be the exciting factor. The role played by hematoporphyrin in cases of lupus erythematosus due to light sensitivity is most interesting; exactly what happens when an excess of hematoporphyrin is found in the urine is as yet debatable. It is known, however, that Meyer-Betz (*Deutsches Arch. f. klin. Med.* **112**:476, 1913) became seriously ill from severe reactions to actinic light after the injection of this pigment and that white mice into which Hausmann (*Biochem. Ztschr.* **20**:276, 1910) injected hematoporphyrin promptly died, with characteristic symptoms, on exposure to light. Control animals kept in the dark showed no symptoms. Black mice could not be sensitized. It would seem, therefore, that an excess of hematoporphyrin in the system seems to coincide with an increase in light sensitivity. It would seem worth while to determine the amount of hematoporphyrin in the urine of Dr. Wise's patient. The appearance of the patches on nonexposed parts of the body does not militate against the diagnosis of disseminate lupus erythematosus caused by actinic light. I recall a patient with lupus erythematosus of the discoid type who inadvertently was given an excessive exposure of radiation from an air-cooled quartz mercury vapor arc lamp on cutaneous areas not affected by the disease and normal in appearance. New outbreaks of lupus erythematosus soon appeared, not only on the spots exposed but on those not exposed.

DR. HOWARD FOX: A patient could have a disseminated type of lupus erythematosus of this extent without constitutional symptoms, for the time being at least. However, I have never seen an example of lupus erythematosus disseminatus with such sharp borders as this eruption presents. From a distance the condition looks much like pityriasis rubra pilaris, but on close examination one fails to see the typical papules of this disease. Pityriasis rubra pilaris is one eruption that may have cleancut sharply demarcated borders, and another is the one mentioned by Dr. Hopkins, a pellagroid eruption due to some dietary deficiency. I think the possibility of a vitamin B_1 deficiency is worth considering.

DR. MAURICE J. COSTELLO (by invitation): If this eruption is acute lupus erythematosus of the disseminated type, a normal leukocyte count is unusual. A leukopenia is almost a constant accompaniment of this disease.

DR. GEORGE MILLER MACKEE: I have seen the sharp margins mentioned by Dr. Fox occur in disseminated lupus erythematosus, although the occurrence is rare. In addition to the large areas of dermatitis, this patient has bullae, vesicles and crusts. A Senear-Usher syndrome and dermatomyositis should be considered.

A Case for Diagnosis (Recurrent Dermatitis Herpetiformis Repens?).
Presented by DR. GEORGE C. ANDREWS.

G. G., a woman aged 34, a school teacher, is presented with a recurrent bullous eruption of the neck, axillas and inner aspect of the thighs. The condition first

appeared five months ago, and each recurrence has affected the same sites. In the early phase of the eruption the skin is erythematous and there are many bullae, some of which are as large as a 25 cent piece. There is considerable itching at this time. The bullae soon rupture, leaving denuded spots which crust. The skin then becomes dry and shows some exfoliation throughout the lesions. Each recurrence has gone through this cycle.

The condition usually responds well to fractional roentgen ray therapy (75 r, unfiltered, once weekly) and local treatment (cold boric acid compresses and 5 per cent naftalan ointment). The condition will remain clear for a period of days, only to recur in the same sites and go through the described cycle.

There was a strongly positive cutaneous reaction to a patch test with finger nail polish. Removal of nail polish failed to influence the course of the eruption. There were also positive cutaneous reactions to seven pollens, ten foods and five inhalants. It has not been proved that these substances or any other allergens have had any influence on the eruption.

There is a vague history of past streptococcic infection. The focus of this infection has never been discovered, but the patient has been given streptococcus vaccine for many months by another physician. Cultures of material from cutaneous lesions failed to show pathogenic bacteria or fungi. Monilia albicans was cultured from the corners of the mouth. The blood count was normal. Urinalysis revealed many long chain streptococci.

This condition seems to correspond with that described in the article "Recurrent Herpetiform Dermatitis Repens" (Ayres, S., Jr., and Anderson, N. P.: ARCH. DERMAT. & SYPH. **40**:402-413 [Sept.] 1939).

DISCUSSION

DR. EUGENE F. TRAUB: The condition in this case, to judge from the history and the histologic studies, belongs in that group of diseases described by Hailey and Hailey under the title "Familial Benign Chronic Pemphigus" (*South, M. J.* **33**:477, 1940), an example of which I showed at the last meeting. The eruption does not look exactly like that in any of the other cases described, but if it is a chronic bullous condition and if the presenter believes it conforms to that described by Ayres and Anderson, then it is my opinion that it would be proper to include it in the category of diseases described by Hailey and Hailey. As I stated at the last meeting, I object only to the name pemphigus and again suggest the designation familial benign chronic bullous dermatosis.

DR. FRED WISE: It is the generally accepted view that the case reported by Ayers and Anderson belongs in the same group as those of Hailey and Hailey and Pels and Goodman, who described the eruption as a bullous form of Darier's disease. I have observed 2 similar cases, as well as those of Hailey and Hailey, and they all resemble each other at various times; the histologic picture seems to be fairly uniform in all. I believe that the eruption possesses some histologic features resembling Darier's disease but that it bears no clinical relation to Darier's keratosis follicularis.

DR. HOWARD FOX: I agree with Dr. Wise that the three diseases under discussion are all the same. I believe it is agreed that the condition in the cases reported by Hailey and Hailey and by Pels and Goodman is the same as that described by Ayers and Anderson.

DR. GEORGE C. ANDREWS: This patient lacks a familial history and in addition has had the disease only five months, which is a shorter time than that in the other cases being discussed. As I understand it, these conditions show definite dyskeratosis histologically.

Urticaria Pigmentosa and Lichen Planus of Simultaneous Onset. Presented by Dr. George C. Andrews.

E. N. R., a Mexican aged 37, a clergyman, was first seen by me on Jan. 14, 1941, with a generalized eruption of about eight months' duration. It first appeared as brown spots on the neck and gradually spread, involving practically all the skin except that of the scalp, forehead, palms and soles. The lesions on the wrists appeared simultaneously with the eruption on the body. There have been no subjective symptoms except occasionally mild itching.

There was no evidence of allergy in the history of the patient or in that of his family or of foci of infection. The patient had measles and yellow fever in

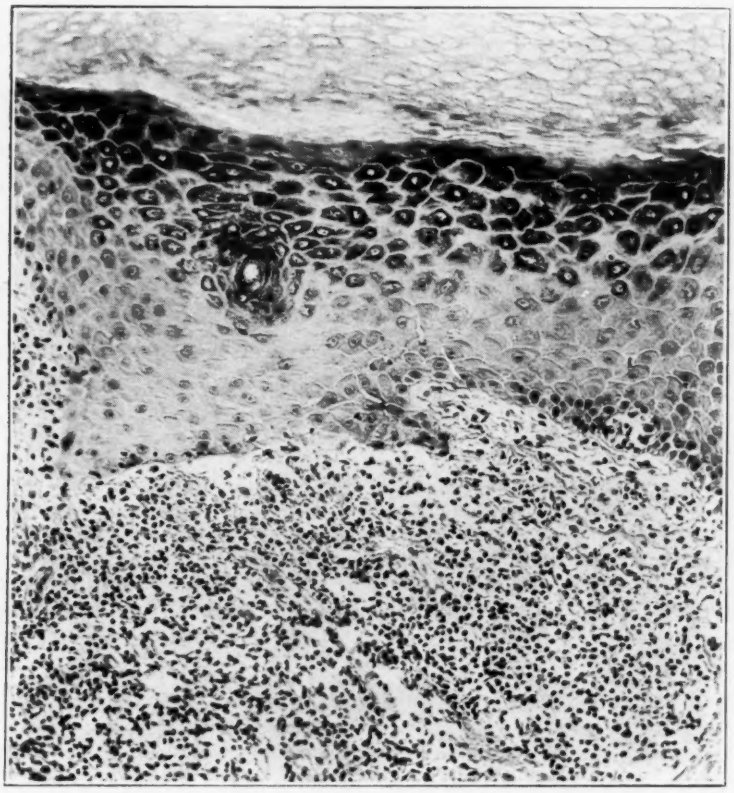

Fig. 1.—Hypertrophic lichen planus, showing thickening of the horny layer, increase in the granular layer, acanthosis, disturbance in the basal cell layer and a bandlike infiltrate in the upper part of the cutis.

early childhood and typhoid fever seventeen years ago. During recent months there have been chilly sensations (with an oral temperature of 99.2 F.). The family physician suspected malaria, but blood smears failed to show organisms. The general health has been good except for nervousness.

Examination shows a widespread brownish, macular eruption on the lower part of the face, neck, chest and abdomen and on both upper and lower extremities, with a bilaterally symmetric distribution on the extensor surfaces of the upper extremities and on the abdomen. The individual lesions are brownish macules,

round to oval, and vary in size from 1/16 to 1/4 inch (0.15 to 0.6 cm.). There is definite whealing when the macules are vigorously rubbed.

The anterior surfaces of the wrists show annular violaceous lesions composed of confluent hypertrophic flat-topped papules typical of lichen planus. On the buccal mucosa, on either side, there are many tiny pinpoint-sized white papules arranged in a lacelike pattern.

No treatment has been given except a few injections of calcium.

Histologic section from the lesion on the anterior surface of the right wrist showed an increase in the horny layer, an increase in the granular layer and acanthosis of the epidermis. There were areas which showed a disturbance of the

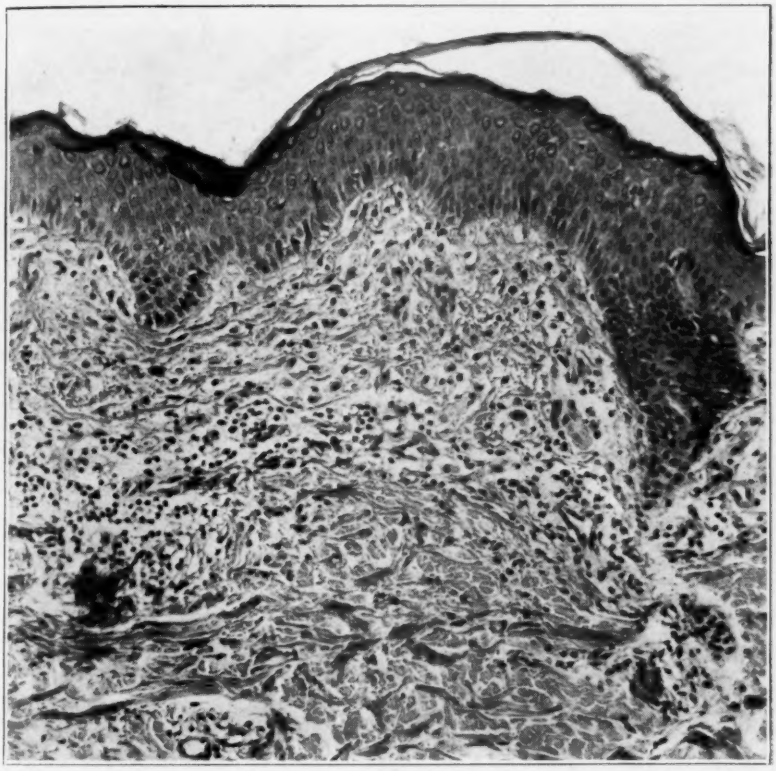

Fig. 2.—Urticaria pigmentosa (low power magnification), showing distribution of mast cells in the upper part of the cutis.

basal cell layer. The upper part of the corium showed a rather uniform bandlike infiltrate composed of mononuclear lymphocytic cells. The histologic diagnosis was lichen planus hypertrophicus.

Histologic sections of a small pigmented lesion from the back showed a slight hyperkeratosis, a slight acanthosis and edema. The granular layer was fairly narrow. The striking changes were seen in the upper part of the corium. These were fairly well localized. The blood vessels were dilated and the walls somewhat thickened. This thickening was due chiefly to a swelling of the endothelial lining. Surrounding the blood vessels were edema and an infiltration of small mononuclear cells which appeared to be lymphocytes. An occasional eosinophil was distinguished.

Most characteristic, however, were the mast cells which were included in the infiltration. In some sections they were not strikingly numerous. The examination of numerous sections, however, disclosed a few in which their numbers pointed definitely to the diagnosis of urticaria pigmentosa. The metachromic cytoplasmic granules of the mast cells were demonstrated by the use of polychrome stains. The histologic diagnosis was urticaria pigmentosa.

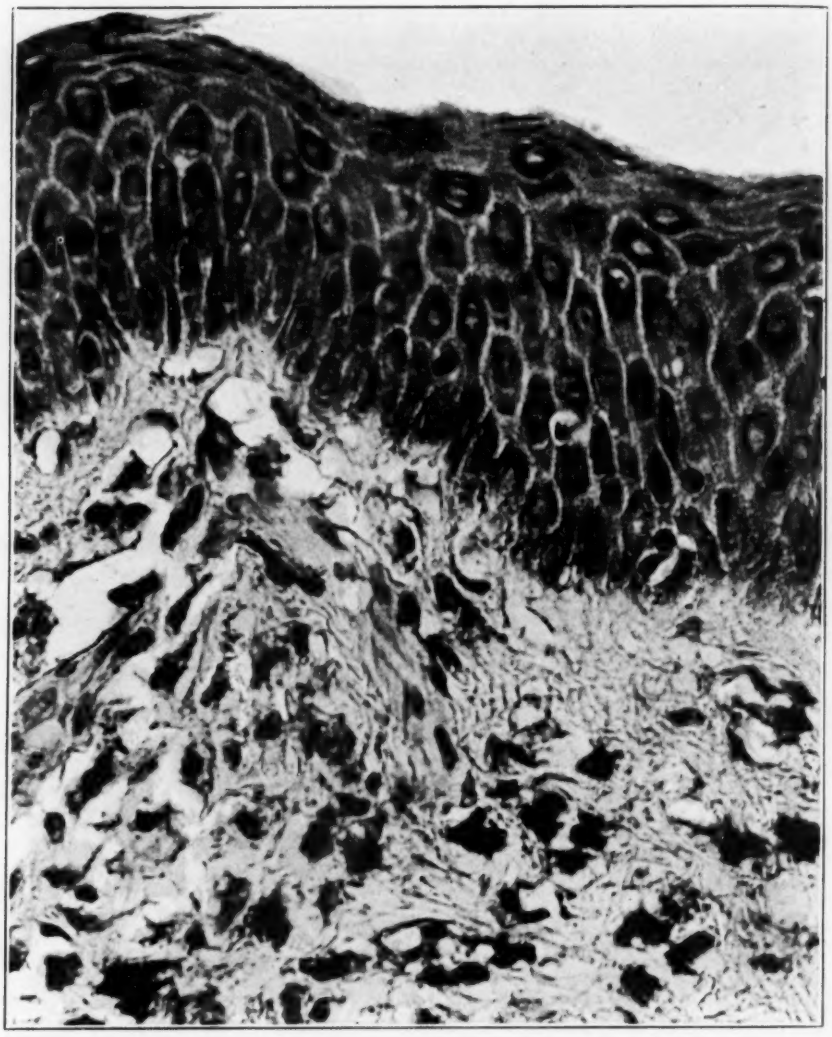

Fig. 3.—Urticaria pigmentosa (high power), showing details of mast cells in the upper part of the cutis.

A Case for Diagnosis (Prurigo Mitis?). Presented by Dr. Howard Fox.

S. G. O., a widow aged 49, has suffered for the past four years from a generalized eruption associated with intense itching. The eruption has been most severe during the summer months and until this year had almost disappeared during cool weather. It began on the nape of the neck, the patient ascribing its

origin to a burn from treatment by diathermy. The eruption then spread to the face, trunk and extremities. There has never been any grouping of the lesions, pigmentation or appreciable scarring. The lesions have never coalesced and formed patches. Dermographia is fairly intense. The feet and the mucous membranes of the mouth are normal.

An operation for gastroptosis was performed twenty years ago. For many years she has suffered from digestive disturbances. She was formerly treated for pyorrhea, but at present her teeth are in fair condition. She uses tobacco and alcohol moderately. Menstruation stopped five years ago. When I first saw her, in June 1940, no adenopathy was apparent. This appeared later in the axillas, groins and neck and, at one time, suggested Hodgkin's disease. She was then hospitalized for a week and was given sedatives and antipruritic remedies, with great improvement. At no time could the liver and spleen be palpated. Examination of the blood on four occasions showed the hemoglobin to vary between 85 and 90 per cent, the erythrocytes between 4,000,000 and 4,500,000 and the leukocytes between 7,800 and 10,600. There was always a mild relative lymphocytosis, the polymorphonuclear leukocytes varying from 41 to 48 per cent. A roentgenogram of the chest showed no mediastinal growth or evidence of tuberculosis. The sedimentation rate of the blood (Westergren) was 10 mm. at the end of one hour. The patient was previously given eighty-four scratch tests, with twelve positive reactions; no benefit, however, resulted from avoidance of contact with substances giving positive reactions. She failed to be benefited by salves, roentgen rays, autoserotherapy and five intravenous injections of neoarsphenamine. She was also given vitamin B complex and intramuscular injections of liver extract, the latter being of some apparent benefit.

DISCUSSION

DR. PAUL E. BECHET: The patient shows a few definite urticaria-like nodules, some of which have a surrounding erythematous halo, but the great mass of lesions are frankly excoriations, many of which seem scooped out. There is much scarring. The patient exhibits definite neurotic stigmas. Because of this fact, the pruritus from her urticaria is greatly exaggerated and causes her to scratch and pick at her skin to a far greater extent than would a person with a normal nervous balance. I believe that she presents both urticaria and neurotic excoriations.

DR. RAY H. RULISON: I believe the condition is a papular urticaria.

DR. HOWARD FOX: I am glad no one considered this condition to be a papulonecrotic tuberculid. I accept the diagnosis of papular urticaria, which is practically the same as mild prurigo.

Rosacea-Like Tuberculid of Lewandowsky. Presented by DR. GEORGE C. ANDREWS.

B. M., a woman aged 38, was previously presented before the New York Academy of Medicine, Section of Dermatology and Syphilis, on Jan. 7, 1941 (ARCH. DERMAT. & SYPH. **44**:280 [Aug.] 1941).

DISCUSSION

DR. GEORGE MILLER MACKEE: Dr. Andrews has had the advantage of seeing the patient a number of times and studying the case carefully; so I hesitate to disagree with his diagnosis. But rosacea-like tuberculid of Lewandowsky rarely occurs on the nose. Usually the center of the face escapes in that disease. Furthermore, the tiny nodules in this case disappear entirely under diascopic pressure, which does not occur in this form of tuberculid. Moreover, the histologic structure is not that of rosacea-like tuberculid. I favor a diagnosis of rosacea.

DR. MAURICE J. COSTELLO (by invitation): The eruption has improved since the patient was last presented. That fact and the exacerbation after injections of

tuberculin followed by improvement are in favor of the diagnosis of rosacea-like tuberculid of Lewandowsky.

DR. PAUL E. BECHET: Erythema is absent. The lesions consist of multiple reddish yellow nodules, the size of a small pinhead. On diascopic pressure some of the nodules disappear, but a considerable number do not and a distinctly yellow center can be discerned. A few of the latter seem capped with small pustules or crusts. In my opinion the evidence favors the diagnosis of lupus miliaris disseminatus faciei rather than that of rosacea-like tuberculid of Lewandowsky.

DR. J. GARDNER HOPKINS: I should like to ask Dr. MacKee about the criteria for the diagnosis of Lewandowsky's tuberculid. As I understand it, one would exclude conditions without tuberculous structure.

DR. GEORGE MILLER MACKEE: I would refuse to make a diagnosis of rosacea-like tuberculid histologically unless there was a tuberculoid structure.

Without histologic confirmation—meaning a tuberculoid architecture—it may be impossible to make an unequivocal diagnosis of Lewandowsky's disease, and I understand that the histologic picture in this case was not tuberculoid. Clinically, there should be tiny nodules, often capped with minute pustules, and erythema around the periphery of the face, tiny pits and failure of the papules to disappear under diascopic pressure. The tuberculin reaction is usually positive. Acne vulgaris at times shows a somewhat tuberculoid structure. According to some authors, a type of acne vulgaris is caused by tuberculosis. In a case of this kind it is claimed that exacerbation and improvement can be caused by injections of tuberculin.

DR. EUGENE F. TRAUB: Regarding the tuberculin reaction in this case and the response to it, I think it was Van Studdiford who reported a series of ordinary cases of acne in which tuberculin treatment was given and in which the same thing held true; so I do not believe that the response to treatment can be accepted as deciding the issue one way or the other.

Pemphigus Vulgaris. Presented by DR. GEORGE C. ANDREWS.

J. F. T., a dairyman aged 65, has had a bullous eruption on the anterior portion of the legs for the past eight months. The lesions appear as blisters on otherwise normal skin, but sometimes there is an erythematous base. These eventually rupture, crust over and heal, and new blisters form. The bullae, though superficial, have a tough wall. The eruption has remained localized, and there are no subjective symptoms.

There is no history of ingestion of drugs or of allergy. The patient has mild diabetes, which is controlled by diet. He has chronic sinusitis, and the teeth are in need of repair. He was formerly a heavy drinker.

Bacteriologic examinations of the lesions have revealed no organisms. Mycologic examinations have given negative results. Examination of the blood showed: 4,430,000 erythrocytes, 92 per cent hemoglobin and 12,000 white blood cells. The differential count revealed 66 per cent polymorphonuclear leukocytes, 32 per cent lymphocytes, 1 per cent eosinophils and 1 per cent basophils.

The urine was normal, and the blood sugar amounted to 100 Gm. per hundred cubic centimeters.

An internist who completely examined this patient added the following information:

"The patient's heart is hypertrophied and is placed transversely in the chest, and there are probably roughening and sclerosis of the aortic valve and aorta. Probably he has cirrhosis of the liver, although this cannot be proved. His abdomen may even contain fluid. His condition in general is not good. Later, when he has no fever, he should have a basal metabolism test."

Treatment has consisted of boric acid compresses, tannic acid spray, small doses of acetarsone, sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) and two fractional doses of roentgen rays (75 r, unfiltered, at weekly intervals) to the legs.

DISCUSSION

DR. FRED WISE: The eruption is not a true pemphigus. I think it is a pemphigoid eruption of unknown cause, confined to the legs. Eruptions of this form are referred to in the foreign literature as pemphigus isolatus.

DR. EUGENE F. TRAUB: This eruption, located only on opposing surfaces of the legs—areas easily accessible—is in my opinion a dermatitis factitia. I followed a somewhat similar case for a long time. My patient was producing the eruption with an intent to deceive; it consisted of blebs on normal skin, with but little artificial appearance, but he finally admitted that they were produced by steam from a tea kettle.

DR. A. BENSON CANNON: I agree with Dr. Wise that the condition is not one of pemphigus for the reasons enumerated and because of the added fact that the patient is a gentile. I have under observation at present an elderly man who has been annoyed with a similar bullous eruption that I was able to trace to the use of iodized salt. He was not in good physical condition; he was suffering from hypertension and had been taking from eight to twelve alcoholic drinks a day for twenty years, a factor I suspect of favoring the retention of iodide.

DR. GEORGE MILLER MACKEE: Localized pemphigus is exceedingly rare except in the mouth and very occasionally about the eyes. I think Dr. Andrews will have to exclude bromoderma and iododerma and, by careful cultural tests, fungous eruptions, in addition to ruling out the possible diagnosis mentioned by Dr. Traub. I do not think the condition is pemphigus.

DR. HOWARD FOX: I might add that the man has not lost weight.

DR. PAUL E. BECHET: The absolute symmetry of the lesions on both legs, as well as the duration and the limitation of the eruption to the legs, militate against the diagnosis of pemphigus. I am inclined to believe that some form of contact sensitivity is responsible for the eruption, such as woolen socks, dyed clothes or cleaning fluid. The condition is not an artefact in the sense of being an artificially produced eruption.

DR. HOWARD FOX: The exact symmetry is against the diagnosis of an artefact in my opinion. A patient with such a condition does not take pains to make the eruption symmetric unless he is extremely clever.

DR. EUGENE F. TRAUB: By calling the condition dermatitis artefacta I meant not that it was necessarily induced deliberately or with intent to deceive but that it was probably produced more or less accidentally, hence artificially or physically.

DR. GEORGE C. ANDREWS: The patient had been taking iodized salt and was advised to stop eight weeks ago. He has been in the hospital for ten days. On admission his blood pressure was about 190. While he has been in the hospital, his diabetes has been controlled by diet; he has not been given alcoholic beverages; his blood pressure has been somewhat lowered, and his teeth, tonsils and sinuses have been treated. I believe that he has an early stage of pemphigus, which later may develop more extensively.

A Case for Diagnosis (Rhinoscleroma?). Presented by DR. A. BENSON CANNON.

A. R., a white woman aged 64, a widow, is presented from the Vanderbilt Clinic. The patient was first seen in October 1940, at which time she complained of a swelling of the nose which had persisted for six years.

The past personal history is noncontributory except for attacks of asthma and hay fever, which have recurred at intervals for the past twenty years. The general health is excellent. There are no subjective symptoms.

The present disease began about six years ago as a small reddish lump on the left side of the nose, just above the ala, and gradually spread until in about a year the swelling had extended into the septum on both sides. Since the onset the patient has been studied by a number of dermatologists, both in this country and in England, and the condition has been variously diagnosed as furunculosis, lupus erythematosus, syphilis, tuberculosis and rhinoscleroma.

Histologic examination of tissue from the septum in 1932 showed an inflammatory condition, but a later examination was reported as showing probable rhinoscleroma. Numerous bacterial cultures have been made in the past, all of which were sterile.

The patient has had the maximum amount of irradiation with both radium and roentgen rays and has also been treated with solid carbon dioxide and by electrodesiccation.

The physical examination showed no abnormality except the nasal condition.

In spite of various treatments received during the past six years, the condition of the nose has not improved. The lesion has continued to spread, until in October 1940 it involved both sides of the nose and the septum, the adjacent portions of the cheeks and the lower eyelids. The nose has increased to almost twice its normal size and is flattened and fused with the cheeks. The septum is also increased in size. The entire area, which appears swollen and nodular, is painless and hard. The skin over the nose is white shading to pink, and on the bridge and tip it appears shiny and telangiectatic. It has become fused with the skin of the cheeks, which have become thickened, bluish and sharply demarcated. The swelling has extended from 1 to 1½ inches (2.5 to 4 cm.) over each cheek and over the bridge of the nose to the eyebrows. The lower lids are swollen and darkened.

Roentgen ray examination of the nose showed a calcified margin around the infiltrated mass. The sinuses were normal. Roentgenograms of the skull, chest and long bones showed no abnormalities.

Repeated cultures of material from the septum, as well as cultures of serum from biopsy material and of serum taken by puncture from the affected parts, were all sterile. Animal inoculations gave negative results. The Wassermann reaction of the blood was negative, and the blood count and the urine were normal.

Histologic examination of tissue removed from adjoining parts of the nose and cheeks showed probable rhinoscleroma.

Treatment has consisted of blistering applications of solid carbon dioxide, intramuscular injections of sterile milk and sulfanilamide by mouth. The results have been striking: the nose has become much smaller and smoother. The bluish swelling of the adjacent parts of the cheeks has disappeared, as has the swelling of the lower lids. The partial obstruction of the nares has also become much less.

DISCUSSION

DR. GEORGE C. ANDREWS: I think the presentation is conclusive, and I agree with the diagnosis of rhinoscleroma.

A Case for Diagnosis (Lichen Scrofulosorum?). Presented by DR. A. BENSON CANNON.

E. T., a white woman aged 58, first came to the Vanderbilt Clinic in December 1932, complaining of a generalized eruption of two months' during.

The patient has been married for twenty years, and her husband and two children are living and well. There have been many induced abortions.

She had an appendectomy at the age of 20, followed by pneumonia. She had a partial oophorectomy nine years ago. A tuberculous right kidney was removed in April 1932 and an operation for an anal fistula was performed in August 1932. She suffered from tuberculous pleurisy two months later. In 1938 she had con-

junctivitis and otitis media, apparently of tuberculous origin, although no acid-fast bacilli could be found in the smear. In August 1940 she had an acute otitis media of the left ear which lasted one month.

When first seen in the dermatologic service at Vanderbilt Clinic in December 1932, the patient had groups of pinhead-sized or smaller raised yellowish red scaly papules on the trunk and scalp and reddish brown infiltrated scaly papules on the extremities. She said they had been there for the previous two months. Histologic examination of the lesions on the trunk and scalp was reported as showing lichen scrofulosorum, and of those on the extremities, dermatitis.

In 1933 the patient appeared again with a diffuse eruption under the breasts, atrophy of the tongue with loss of papillae, and atrophy of the vaginal wall. A tentative diagnosis of Plummer-Vinson syndrome was made. She was treated at Rockeller Institute for the next six months with intramuscular injections of liver and with vitamin B complex by mouth. The condition of the mouth and vagina improved greatly, and some of the lesions on the back also disappeared.

In 1937 the patient returned to Vanderbilt Clinic with a reddish, rolled, slightly scaly, semicircular, nodular lesion under the chin, which closely resembled a sarcoid or gummatous nodule. Histologic examination showed it to be a miliary tuberculid. The patient was given a course of eighteen injections of bismo-cymol during the next six months and simultaneously received ultraviolet irradiations over the involved areas at weekly intervals for the following year, with occasional rest periods. After eight injections of the bismuth compound the nodular eruption on the chin disappeared entirely, and the ulcers on the thigh and the eruption on the legs and pubis improved greatly. From December 1938 to May 1939 she received another course of seventeen injections of a bismuth compound, as well as carbon arc light treatments, although with comparatively little resultant change in the cutaneous eruption.

In January 1939 Monilia albicans was found in cultures of material from the mouth and stools.

Histologic examination of a section from the lesion on the leg in February showed lichen scrofulosorum, but it was noted that in view of the good response to bismuth therapy syphilis would have to be considered as a possible diagnosis.

In May 1939 she received three small doses of arsphenamine, which greatly aggravated the eruption on the leg. The spinal fluid was normal in all phases at that time, and the reactions to the Wassermann and precipitation tests of the blood were negative.

In January 1940 a dystrophy of the nails developed, with scaling at the margins. Cultures of scrapings from the nails showed Trichophyton gypseum.

In August 1940 she was given sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) for the treatment of an acute otitis media of the left ear. A rash developed. Two months after this rash cleared up she suffered a recurrence of the earlier lichenoid lesions on the trunk and extremities.

In January 1941 two intracutaneous injections of 0.1 cc. each of old tuberculin, in a dilution of 1 : 1,000,000 and of 1 : 100,000, elicited negative reactions. The lesions on the legs became much larger and redder after the second injection of tuberculin.

Histologic examination of tissue from a follicular papule on the leg in January showed lichenoid tuberculosis.

The patient now presents lesions limited to the lower extremities, the groin and the pubic region. These lesions are of the following three types: 1. Those on the legs—chiefly on the front and sides—consist of erythematous, brownish red, macular, scaly lesions and plaques, ranging in size from that of a pea to that of a 25 cent piece, which have resulted from the coalescence of grouped pinhead-sized scaly papules. 2. On the anterior and lateral aspects of the thighs and in the groin are shiny red lichenoid papules, varying in size from that of a number 8 shot to that of a pea. 3. In the folds of the skin of the pubic region there are red macular scaly intertriginous lesions.

The histologic diagnosis was lichenoid tuberculosis and the clinical diagnosis tuberculosis cutis.

DISCUSSION

DR. HOWARD FOX: The lesions on the legs, around the umbilicus and in the groins did not look like any form of tuberculosis with which I am familiar. They suggested to me a superficial type of psoriasis. There was not much of a lichenoid eruption that I could see. The lesions did not have the color or appearance of lichen scrofulosorum. Furthermore, lichen scrofulosorum, in adults at least, is an exceedingly rare disease in this country.

DR. GEORGE MILLER MACKEE: At first I had the same impression as Dr. Fox, namely, that the condition was a psoriasiform eruption if not psoriasis. In an informal discussion Dr. Cannon assured me that while there is no follicular element now and no papules, the eruption did originally consist of grouped papules; they have been flattened by therapy, leaving scaly patches. That picture is compatible with the diagnosis. Histologically, I found a large area of degeneration in the cutis but no giant or epithelioid cells. I think that Dr. Cannon's diagnosis is correct in spite of the unsatisfactory clinical picture as presented today.

DR. J. GARDNER HOPKINS: Just from the point of view of terminology, when Jadassohn tried to bring some order to the classification of cutaneous tuberculosis he classified lichen scrofulosorum as tuberculosis lichenoides.

DR. EDWARD R. MALONEY: I certainly would not make that diagnosis of a superficial patchy eruption in a woman of 60. I do not believe this disease is very often found in an adult of that age, and the patient's condition does not look like tuberculosis to me.

DR. A. BENSON CANNON: I agree with Dr. Fox and Dr. MacKee that the lesions on this patient's legs are not at all characteristic of tuberculosis. They are mostly brownish red scaly plaques, but the initial lesions were follicular papules the size of a small pinhead that appeared in clusters and later became fused into the plaques present today. She now has split pea–sized red dry lichenoid papules in the groins and a few groups of the lichen-scrofulosorum-like papules on the thighs. The large lichenoid lesions in these areas more closely resemble sarcoid than they do lichenoid tuberculosis. The patient has been observed at the Vanderbilt Clinic for eight years, during which time she has had biopsy specimens taken at three different times. These all showed a tuberculous structure of one sort or another. The patient has proved tuberculosis of the kidneys, lungs and pleura.

A Case for Diagnosis (Sycosis Vulgaris in a Woman?). Presented by DR. EUGENE F. TRAUB.

Mrs. S. S., aged 40, a housewife, born in Russia, presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, complains of an eruption on her chin which has been present for about two years. The patient has been in the habit of epilating superfluous hair from her chin with a tweezer every two weeks. The entire chin is involved. There are firm inflammatory nodular lesions, varying in size from that of a large pinhead to that of a pea, some of which show a yellowish point on their summits suggesting pustulation. Some of the lesions appear to be mildly inflammatory papules. The skin is red and scaly.

Graded tuberculin tests showed the following results: with a 1:1,000,000 dilution, a plus-minus reaction; with a 1:100,000 dilution, a 2 plus reaction, and with a 1:10,000 dilution, a 2 plus reaction. A complete blood count was normal, as was the urine. The Wassermann reaction of the blood was negative. Culture of hairs from infected lesions showed no fungous growth. Histologic examination, by Dr. Else A. Barthel, revealed the following information: The section showed a diffuse cellular exudate extending down to and between the muscle fibers. In places the epidermis was atrophic. There was an inflammatory exudate that completely surrounded the hair follicle and extended up to the epidermis. In this area the cellular exudate consisted of granulation tissue, including new blood vessels, lymphocytes and numerous eosinophils. The microscopic diagnosis was folliculitis.

DISCUSSION

DR. HOWARD FOX: The condition in this case does not look to me like sycosis. I could not see any follicular pustules or even the eczematous appearance of chronic sycosis. The lesions look like papules which might possibly be due to one of the drugs of the halogen group. Dr. Traub said sycosis in a woman was unique. I have a photograph taken by my father of a woman with hypertrichosis showing a patch of sycosis with typical follicular pustules.

DR. PAUL E. BECHET: I do not believe that this condition is sycosis in the true definition of that disease. Pustular folliculitis is not present. The lesions apparently consist of papules and nodules, without follicular pustules. The skin over the area is rough and thickened. I suggest that pumice stone may have caused this eruption. I have observed changes similar to those in this patient after long-continued use of pumice stone for the relief of hypertrichosis. If such a history cannot be elicited, I should consider the possibility of a bromide or iodide eruption.

DR. RAY H. RULISON: The woman had a series of epilations by electrolysis. I think the nodules are more fibrotic than pustular.

DR. J. GARDNER HOPKINS: Does not pulling of the hairs explain the whole condition? One often sees pits, scars and even pustules at times where the hair growing back gets caught under the epidermis.

DR. JEROME KINGSBURY: I think the condition is secondary to a mechanical inflammation of the follicles. It would be improper to refer to it as sycosis.

DR. GEORGE MILLER MACKEE: I do not think the condition is sycosis vulgaris. I do not think there are any nodules and papules. The elementary lesion is a thick-walled pustule, a type of lesion which looks like a lesion of so-called cystic acne. One frequently sees acne and acneform eruptions limited entirely to the chin, and I am more inclined to think it is either the condition mentioned by Dr. Hopkins or cystic inflammatory acne limited to the chin. Of course bromoderma and perhaps iododerma must be eliminated.

DR. EUGENE F. TRAUB: To answer Dr. Bechet about pumice, the patient stated that the only thing she has done is to pull or tweeze the hairs. In regard to acne, as I mentioned, there were three different biopsies performed in two years, and the histologic picture certainly was not that of acne as far as I could ascertain. The lesion was simply a chronic inflammatory nodule, usually with a hair follicle involved in the process, so it would be correct to call the condition a folliculitis, I suppose. The question of iodides and bromides has been investigated, and they have been excluded as possible causes, as far as the history and the examination of the urine are concerned.

Mycosis Fungoides (the Infiltrative Type, of Sixteen Years' Duration).
Presented by DR. EUGENE F. TRAUB.

B. G., a woman aged 40, was first seen about thirteen years ago at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. She presented an eruption on the face which resembled erysipelas but which was diagnosed histologically as mycosis fungoides. She responded promptly to roentgen ray therapy, and many recurrences since that time on various parts of the body have responded to that treatment. Recently the large plaques in the axillas and on the trunk have failed to do so, even though in some instances atrophy and permanent loss of hair have resulted from the therapy. She has received a total of sixty or seventy doses of 75 r each (¼ skin unit) of unfiltered roentgen rays.

DISCUSSION

DR. EUGENE F. TRAUB: A rather interesting point is that the mycosis fungoides developed when the woman was 25 or 26 years old, and immediately after the appearance of a large erythematous plaque involving one side of the face, infiltrated lesions developed, which, while they were not real tumors, were so infiltrative that

they suggested early tumor formation. Such lesions have been present continuously for over fifteen years; so the disease has been not in just the premycotic stage but in the premycotic and infiltrated stages from the start.

DR. J. GARDNER HOPKINS: Is it not justifiable in a case of a disease as serious as mycosis fungoides to administer roentgen rays even to the point of producing a radiodermatitis if necessary? The disease is malignant and eventually fatal, and I do not think the fear of radiodermatitis should prevent the use of sufficient therapy to control the disease.

DR. A. BENSON CANNON: The only patient with mycosis fungoides in the tumor stage that I know of who was successfully treated received arsenic in addition to irradiation. I urge the giving of arsenic to this patient.

DR. HOWARD FOX: I believe Dr. Fordyce had successful results from the administration of arsphenamine in cases of mycosis fungoides.

DR. A. BENSON CANNON: Dr. Fordyce's patient had multiple fungating tumors that were very large and so numerous that Dr. Fordyce predicted a fatal outcome. Need of irradiation was so urgent that often a tremendous number of tumors had to be treated at one sitting. Such a large amount of radiation was given at each treatment that the patient sometimes had fever, with a temperature of from 102 to 104 F., and felt weak and tired. After receiving weekly injections of arsphenamine in small doses in addition to the irradiation, the tumors were entirely cleared up, and the patient gained 40 pounds (18 Kg.) in weight. She has remained well for about eighteen years and visits me almost yearly for observation.

Mycosis Fungoides (with Large Single Tumor). Presented by DR. EUGENE F. TRAUB.

F. K., a man aged 52, born in the United States, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Jan. 13, 1941. He presents a generalized eruption of twenty years' duration. It is erythematous, scaly and noninfiltrating and consists of discrete and confluent lesions, some of which resemble psoriasis. Many of the lesions on the trunk, back and chest are pigmented. There is a firm, raised, sharply marginated plaque, deeply infiltrated, 4 inches long and 3 inches wide (10 by 7.5 cm.) on the dorsum of the left wrist. There is pronounced adenopathy in the left axilla.

Two biopsy specimens were taken, one from the wrist and one from the back. The histologic diagnosis of the tissue from the wrist was mycosis fungoides and showed the following changes: In the middle and upper parts of the corium was an infiltrating mass of cells, many of which were large and pale staining and suggested young connective tissue cells. Others had large nuclei with well marked nucleoli. These were usually large cells with a granular pinkish cytoplasm. The walls of the blood vessels were affected with a similar degenerative process; there were occasional round cells that wandered between the stroma cells and occasional plasma cells. The whole picture showed the effect of strong toxin. There were some fragmented nuclei.

Histologic examination of tissue from the back showed a lymphoblastoma.

The urine was normal, and the Wassermann reaction of the blood was negative. The examination of the blood gave the following results: erythrocytes, 4,800,000; hemoglobin, 13.5 Gm., or 81 per cent; color index, 0.84; leukocytes, 12,400, with polymorphonuclear neutrophils 67 per cent, eosinophils 1 per cent, monocytes 5 per cent, lymphocytes 13 per cent and band forms 14 per cent.

DISCUSSION

(The members were in unanimous agreement with the diagnosis.)

Lichenoid Arsphenamine Dermatitis, with a Histologic Picture of Lichen Planus. Presented by DR. J. FRANK FRASER.

H. J., a Negro aged 40, had pain accompanied by redness in the left eye, which developed in March 1940. The following month he attended the ophthalmic clinic

of Lincoln Hospital, where the condition was diagnosed as iritis. The Wassermann reaction of the blood at that time was 4 plus. There was no history of an initial lesion or other signs of syphilis.

The patient was given intravenous injections of arsphenamine, beginning with 0.3 Gm. and increasing to 0.6 Gm. After the fifth injection an eruption accompanied by pruritus appeared on the arms and dorsal surfaces of the feet and in the groins. Thinking this was not important, he said nothing about it to the attending physician. After the eighth injection the doctor saw the rash, discontinued giving the arsphenamine and gave five intravenous injections of sodium thiosulfate and sixteen intramuscular injections of a bismuth compound. After the sixteenth injection of the bismuth compound three injections of 0.3 Gm. of neoarsphenamine were given.

The patient consulted me in January 1941, and he was referred to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital.

Examination reveals a violaceous eruption consisting of lichenoid papules and pigmented macular plaques varying in size from 0.05 to 5 cm. Lesions consisting of whitish verrucous-like plaques are observed in the buccal mucosa of both cheeks.

The Wassermann reaction of the blood was 4 plus on January 21.

DISCUSSION

DR. A. BENSON CANNON: I think the diagnosis of lichen planus due to arsphenamine is the correct one. One cannot distinguish lichen planus lesions following arsphenamine dermatitis either clinically or histologically from lichen planus in which there is no history of arsenical intake, but in postarsphenamine dermatitis one often is able to demonstrate the areas of a simple dermatitis in addition to the lichen planus. Lichen planus following arsphenamine dermatitis will clear up under treatment with sodium or calcium thiosulfate, whereas these drugs have no effect in diminishing the lesions of true lichen planus. I do not consider a lichen planus eruption following arsphenamine a contraindication to further arsphenamine therapy, providing one waits a few weeks before resuming treatment.

DR. FRED WISE: Is it the consensus of the society that this man may receive arsphenamine later?

DR. J. GARDNER HOPKINS: Would not the point be that the patient has a serious disease—syphilis—which requires the use of arsphenamine and that the eruption which he has from that drug will never do him any harm?

DR. GEORGE MILLER MACKEE: It appears to be the consensus that arsenic can precipitate herpes zoster and that arsenic can produce a lichenoid eruption that is indistinguishable from lichen planus. This case is one of lichen planus clinically and histologically, and there is no proof of arsenical dermatitis. The lichen planus may be a coincidence in this case. I always discontinue giving arsenic, at least temporarily, when any eruption appears. It should be remembered that, while arsenic does not prevent lichen planus, it is a conventional drug for treatment of this disease. After the patient has been given a rest from arsenic I should not hesitate in this case to employ the drug again cautiously, although the syphilis could probably be treated satisfactorily with a bismuth compound and iodine because the condition is in a late stage.

DR. A. BENSON CANNON: In the majority of instances one can find evidence of an arsphenamine dermatitis in addition to lesions of lichen planus, a fact which aids one in suspecting arsenic as being responsible for the lichen planus. Especially is one apt to see the dermatitis in the axillas, in the flexures of the arms, around the eyes and in the groins, where there are heat, moisture and friction. I think Dr. Fraser is correct in saying that one is unable to distinguish the lichen planus lesions resulting from an arsenical dermatitis, either clinically or histologically, from lichen planus in which there is no history of intake of arsenic.

Morphea. Presented by DR. EUGENE F. TRAUB.

Mrs. J. A. S., aged 49, was presented at the October meeting of this society (ARCH. DERMAT. & SYPH. **43**:1035 [June] 1941).

DISCUSSION

DR. EUGENE F. TRAUB: The original slide was examined at the hospital in Buffalo, and the diagnosis as presented was confirmed. Clinically, there was a question as to whether the condition was morphea-like basal cell epithelioma or morphea. The picture revealed by a recent histologic examination proves it to be an excellent example of basal cell epithelioma, according to Dr. Fraser; so the condition is a morphea-like basal cell epithelioma.

EDWARD R. MALONEY, M.D., *President*

J. GARDNER HOPKINS, M.D., *Secretary*

Feb. 25, 1941

Extensive Alopecia Areata. Result of Treatment. Presented by DR. PAUL E. BECHET.

J. S., a man aged 36, was previously presented before the New York Dermatological Society on Nov. 23, 1937 (ARCH. DERMAT. & SYPH. **37**:1073 [June] 1938). He is presented again in order to demonstrate the permanence of the therapeutic results attained three and one-quarter years ago and to reiterate the definite advantages of phenol over ultraviolet radiation in the treatment of certain types of alopecia areata, as evidenced by the fact that twelve blistering doses of ultraviolet radiation at intervals of a week had no therapeutic effect but after only five applications of 95 per cent phenol two large patches became completely covered with hair and five others more than half covered. More than three years later there was no recurrence. As the patient was partially bald for four years before the treatment, it is extremely difficult to believe that the complete and permanent return of hair after treatment of only eight weeks was a coincidence.

DISCUSSION

DR. HOWARD FOX: It is extremely difficult to prove cause and effect in the treatment of this capricious disease. I was able to obtain the same results in 2 cases in which almost the entire scalp was involved. I administered eleven blistering doses of ultraviolet radiation to one side of the scalp, screening the untreated side. The hair then returned on the side which had been treated. The same procedure was carried out on the opposite side of the scalp and was followed by a complete growth of hair.

DR. GEORGE M. MACKEE: Years ago I did a little experimental work on alopecia areata. In a number of patients the scalp was treated on one side, the other side being left untreated. My results were different from those obtained by Dr. Fox, for in each case the hair grew just as quickly and just as well in the untreated as in the treated areas. These results were obtained regardless of the method of treatment used—and, incidentally, I used different methods, including ultraviolet irradiation and phenol. I came to the conclusion then that recovery in alopecia areata is spontaneous, and I still think it is. I doubt that topical remedies influence the growth of hair very much. I do not think that Dr. Bechet's case proves anything. The fact that the patient has remained well does not prove anything either.

DR. J. FRANK FRASER: Many patients with alopecia areata recover without any treatment. It would therefore always be well to leave a control area when multiple areas of baldness are treated.

DR. JEROME KINGSBURY: Dr. L. Duncan Bulkley in treating alopecia areata with applications of phenol was probably the first to use the control method. He applied phenol to certain areas and demonstrated to his own satisfaction that the hair returned in the places which were treated and did not return in those left untreated.

DR. PAUL E. BECHET: The points brought out by Drs. Fox and MacKee are to a great extent true, but not entirely so. I admit that the course of alopecia areata is extremely capricious and that I have observed the regrowth of hair without treatment. Then, again, I have observed extensive therapy bring about absolutely negative results. This is especially true in cases of alopecia totalis and of circumscribed alopecia areata in elderly persons, but I do not say that for these reasons all treatment for this dermatosis is useless, for that is the exact opposite of my experience. I do not agree with physicians who claim that the favorable response to therapeutic measures proves nothing, and my disagreement is based on the following facts: Here is a patient who for four years was more than half bald. The alopecia affected the bearded region of the face, and his mustache and eyebrows were greatly thinned. For three months blistering doses of ultraviolent radiation had no effect. Then, after only five paintings with the phenol, twice every two weeks, the bald areas were completely covered with hair, while the untreated areas on the eyebrows and upper lip were as bald as ever. If the return of hair was spontaneous, why did it not also return on the eyebrows and on the upper lip? The ability of phenol to grow hair on the bald patches of alopecia areata has been proved time and time again to my complete satisfaction. In corroboration of Dr. Kingsbury's statement, I have also frequently observed Dr. Bulkley paint one half of a bald area and in many instances have observed hair grow on it while the unpainted half remained entirely bald. I have also had the same experience. I do not claim that phenol is a specific treatment for alopecia areata, but my experience with it for over thirty years has convinced me that it is an extremely valuable agent for certain types of alopecia areata.

DR. GEORGE M. MACKEE: Dr. Bechet has given some very good reasons why phenol is a good treatment for alopecia areata. I agree that different conventional treatments may be beneficial. It is not known whether they are or not. I have had a woman under observation since her childhood, perhaps twenty-five years. She has had repeated attacks of alopecia totalis of the scalp. The condition begins as alopecia areata and becomes total. Her hair has returned time and time again, apparently as a result of treatment, but a few years ago it failed to return, in spite of treatment. She became discouraged and stopped all treatment. The hair returned a few months ago, and she came to show me the results of no treatment at all. If she had been treated, whatever treatment was being used before the return of the hair would have been given the credit. I have had a number of similar cases.

DR. FRED WEIDMAN (by invitation), Philadelphia: In the matter of age, Dr. Pusey (Pusey, W. A.: Principles and Practice of Dermatology, ed. 4, New York, D. Appleton and Company, 1924, p. 1189) stated that the younger the subject with this condition and the smaller the patches, the better the prognosis.

Radiodermatitis. Chronic Ulceration of the Right Leg. Presented by DR. PAUL E. BECHET.

F. W., a man aged 46, received a severe gunshot wound of the right thigh in the World War. After a long time the wound healed with much cicatricial thickening, fibrosis and deformity. In an attempt to ameliorate the extensive scarring,

an unknown amount of radium was used in the spring of 1919. A severe dermatitis ensued, complicated by necrosis of the tissues and the formation of an ulcer. In the summer of 1920 an attempt was made to excise the affected area, but it never healed completely. In 1924, at which time the patient had an active ulcer, he came under the care of the late Dr. Whitehouse. For the ensuing thirteen years he was treated by Dr. Whitehouse at irregular intervals with various local applications, including an occasional painting with silver nitrate. The ulcer seemed completely healed at times but would recur at intervals. When last seen by Dr. Whitehouse, on Nov. 19, 1936, it had entirely healed. The patient first came under my observation on Jan. 11, 1941. At that time he stated that there was a thick crusted area about 5 cm. in diameter at the site of the old ulceration. Several days before this initial visit, an ulcer about 2.5 cm. in diameter with gangrenous edges had made its appearance. On inspection, the ulcer presented a raised, foul-smelling, gangrenous lower edge, with greatly infiltrated borders.

There is much sclerosed scar tissue over the middle of the posterior aspect of the right thigh, with atrophy of the muscle tissue and considerable thinning of the leg. After six weeks of mild local treatment and clipping away of the gangrenous area, the ulcer is now clean, smaller and less deep.

The patient is presented because of the frequent recurrence for twenty-two years of an apparently benign ulcer which followed radiodermatitis.

DISCUSSION

Dr. R. H. Rulison: It seems to me that in a case of recurrent ulceration for so long there is probably so much scar tissue that the circulation is badly interfered with and that if some daring surgeon were willing to take out all of that scar tissue and do skin grafting, the best results would be obtained.

Dr. Jerome Kingsbury: I feel as Dr. Rulison does, that a plastic operation would possibly cure this condition. Simple skin grafts over the ulceration would not be sufficient.

Dr. A. Benson Cannon: I think that the scar, including the ulcer, should be excised and the wound skin grafted, and I see no reason why the skin graft should not take, if properly done. I could not detect any evidence of radiodermatitis. The ulcer impressed me as being a trophic one, a type often seen in scarred areas. Should the patient not permit the operation, I believe that immobilization, keeping the wound clean and dressing with Aloe vera leaf might eventually heal the ulcer.

Dr. Geore M. MacKee: Like Dr. Cannon, I am not convinced that radiodermatitis is present. Assuming, however, that it is, regardless of what treatment may be successful in causing the ulcer to heal, that area will always be a menace, because there is a 25 per cent chance of epithelioma occurring in the next five or ten years. Therefore, if the condition is radiodermatitis, a plastic operation is indicated, in spite of the fact that previous surgical treatment was unsuccessful. Malingering should be definitely eliminated before surgical therapy is instituted.

Dr. Howard Fox: The treatment should be surgical, in my opinion. As has been said, the previous operation may not have been properly performed. An ulcer of this type is a potential source of cancer, not to mention its being a nuisance to the patient. Whether it is already cancerous is difficult to say, and it might be difficult to prove this even by histologic examination. Dr. Weidman has shown conclusively that the borders of certain chronic ulcers may show only hyperplasia histologically, which is often mistaken for epithelioma. I think the ulcer and indurated tissue should be removed by an experienced plastic surgeon. The members present will recall the splendid results obtained by plastic surgical therapy in the case of multiple large patches of lupus vulgaris presented by Dr. Traub. Surgical excision and repair should not be more difficult in this case.

DR. PAUL E. BECHET: In a good light the objective symptoms of radiodermatitis are clearly discernible; atrophy, arterial dilatation and sclerosis are all present. When I first inspected the lesion in this case its borders were greatly indurated, and I was suspicious of a malignant growth. I mentioned the necessity of a biopsy, but the patient objected so strenuously that I temporized for a few weeks and used mild topical remedies. To my surprise, the ulcer greatly improved. When I first saw the patient I suggested excision and plastic surgical repair, but he was reluctant to have this done. I should not consider an artefact, as the patient's psyche is apparently normal. He has means of his own and receives no compensation. He could be treated at the government's expense if he wished, but he has made no attempt to do so for twenty years. He drives a car most of the day, and it might be that the ulcer is subjected to pressure by the automobile seat. I have advised him to use a sponge rubber cushion under the affected leg. I will, of course, try to persuade him to have the lesion excised and a plastic operation done.

Erythema Annulare Centrifugum. Presented by DR. FRED WISE.

D. B., a woman aged 33, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Feb. 25, 1941, with a cutaneous lesion of three months' duration. She gave no history of having had any previous disease of the skin. She had had chorea and the usual childhood diseases. She had been taking quinine frequently until a year ago for irregular and delayed menses. She stated that she had not taken any drugs for an entire year except "cold tablets," which she had taken a few days prior to the appearance of the eruption. Her child has asthma.

The present eruption commenced with a minute white spot in the center of a slightly raised, red, penny-sized zone on the ventral surface of the right forearm. This red zone gradually enlarged peripherally, with central clearing, resulting in a ringlike lesion the size of a quarter within a period of one month. This ring is steadily stretching out, with a simultaneous widening of the border, so that it is now twice the size it was a month ago. It has never shown any signs of regression. It is very pruritic, mostly at night. The itching is confined to the ring and to an area about ½ inch (1.3 cm.) beyond, where it is most intense, which presages the new location of the margin.

The lesion consists of a festoon-shaped incomplete ring, 3 inches (10 by 7.5 cm.) in size and enclosing a normal-appearing integument. It extends from the volar and inner surface to the middle of the dorsum of the lower third of the right forearm. Near the upper border, within the ring, on the dorsal surface is an S-shaped detached patch. The border varies from 2 to 4 mm. in width, being more prominent at the proximal half and at the end of the segments which terminate by coiling inward. It is rounded, bluish red, of fairly sharp definition, not scaly and moderately infiltrated. There are three pea-sized satellite lesions close by and on the inside of the edges of the border. Only on firm diascopic pressure do the borders fade, revealing uniform faintly reddish areas.

NOTE.—Histologic examination subsequent to this presentation was reported by Dr. W. Sachs, as follows: Throughout the middle and upper parts of the cutis the vessels were dilated, and about them was a pronounced cellular infiltration. There was a moderate interstitial edema throughout the cutis. The cellular infiltrate was composed chiefly of small round cells. The overlying epidermis showed no important changes. The basal margin was intact. The granular and horny layers were present throughout. The histologic diagnosis was dermatitis.

DISCUSSION

DR. A. BENSON CANNON: I agree with the diagnosis as presented, although it does not convey much to me. I suspect that a drug was responsible; the patient

said that the lesions appeared a week after taking some "cold tablets." One might think of a granuloma because of the hardness and depth of the infiltration.

DR. GEORGE M. MACKEE: I am inclined to agree with the diagnosis, but I think that aberrant granuloma annulare should be considered.

DR. R. H. RULISON: I thought, as Dr. MacKee did, that the condition might be an early granuloma annulare.

DR. JEROME KINGSBURY: I think the diagnosis as presented is the most likely one in this case.

A Case for Diagnosis (Contact Dermatitis Due to Cosmetics? Pityriasis Rosea?). Presented by DR. A. BENSON CANNON.

Miss M. M., aged 28, a bookkeeper, was first seen at Vanderbilt Clinic on Feb. 25, 1941, complaining of a generalized, intensely pruritic, burning and stinging eruption of three weeks' duration. The family history and past personal history were irrelevant. The patient first noticed a red scaly plaque the size of a half-dollar on the back of the right thigh three weeks ago. Within two days there was a generalized eruption, which has remained practically unchanged until the present. She complains of alternating hot and cold sensations in the skin. The patient has been using a commercial bath oil, two different brands of white toilet soap and bath powder for some time. Since the onset of the eruption she has applied only calamine lotion.

Examination discloses a generalized eruption covering the neck, trunk, upper extremities and lower extremities down to the knees. There is a macular erythematous, finely scaling eruption, with large patches and outlying pinhead-sized follicular papules.

No laboratory findings were available as the patient was first seen on the day of presentation.

DISCUSSION

DR. EUGENE F. TRAUB: I believe I agree with Dr. Cannon's original diagnosis of pityriasis rosea, possibly with a superimposed dermatitis of some sort due perhaps to the bath material that she used.

DR. GEORGE C. ANDREWS: I also believe that this case is one of pityriasis rosea with some dermatitis superimposed.

DR. FRED WISE: I agree with Drs. Andrews and Traub.

DR. GEORGE M. MACKEE: I think the condition is an unusually inflammatory pityriasis rosea with considerable confluence. I see no necessity for invoking a superimposed dermatitis, because occasionally one sees pityriasis rosea which is very inflammatory and sometimes even vesicular.

DR. HOWARD FOX: I agree that this condition is pityriasis rosea. One of the most practical articles my father wrote was entitled "A Broader View of Pityriasis Rosea" (*J. A. M. A.* **59**:493 [Aug. 17] 1912). He called attention to the fact that the original description of this disease by Gibert in 1862 consisted of only fifty words. I agree with him that since then the conception of this disease should have broadened. Some dermatologists hesitate to make a diagnosis of pityriasis rosea if the eruption is on the face or extends an inch beyond the wrist or knee. In this case there are more inflammation and confluence than are usually seen, but from the history, location and appearance of the condition I think the diagnosis is unmistakable.

DR. A. BENSON CANNON: The history of the eruption—its having begun as a single, red, scaly patch on the back of the thigh and its having spread within two days over the entire body, the extremities being comparatively free—would make one think of pityriasis rosea. However, when I analyzed the individual lesions, I was unable to find a single one that was typical of pityriasis rosea. The eruption on most of the front and sides of the chest was macular, dry, erythematous, scaly

and fissured, giving a chapped appearance to the skin, whereas the remaining part of the eruption was composed of lesions varying in size from that of a millet seed to that of a pea and larger and of the same appearance as those in the larger patches. There were only a few lesions on the soles, palms, forearms and legs, the body being the main part involved. My first thought was that the condition was pityriasis rosea which had been irritated by treatment, although the patient assured me that she had used only calamine lotion.

Lupus Vulgaris; Basal Cell Epithelioma; Hyperstatic Dermatitis of the Leg. Presented by DR. A. BENSON CANNON.

T. N., a man aged 64, was admitted to the New York City Hospital five weeks ago to be treated for an acute cardiac failure accompanied by edema of the extremities and dyspnea. His family history and past history were essentially normal. He had had a red scaly lesion involving the left cheek for forty years, for which he had been treated both in this country and abroad for lupus. The treatment had been mostly ultraviolet irradiation. He had also noticed a lesion the size of a small pea on the right temple for the past few months. This had increased in size since its onset and become crusted in the center, and it often bled. After the edema of the legs subsided, two weeks ago, he first noticed that the skin from the knees down was brownish, dry, thickened and scaly.

A red, scaly, sharply limited lesion involves the entire left side of the face, with lighter and darker scarred areas scattered over the center. The margins of the lesion are red, irregular, scaly and a bit nodular. Brownish pigmentation is noticeable through a glass slide on pressure.

On the right temple there is a papule the size of a large pea with a central red glandular bleeding surface and rolled, pearly, telangiectatic margins.

The skin on the legs from the knees down is brownish to bluish red, dry, shriveled, hard and scaly, giving somewhat the appearance of amyloid degeneration of the skin.

The Wassermann reaction of the blood was strongly positive, as were the reactions to precipitation tests. The urine and blood count were normal. Histologic examination of tissue removed from the left cheek showed lupus vulgaris and from the lesion on the right temple a basal cell epithelioma.

DISCUSSION

DR. HOWARD FOX: The diagnosis of lupus vulgaris, I think, is evident, even without the aid of a diascope. I do not think the condition in this case could be classed as lupus vulgaris erythematodes (Leloir), which, as I understand it, resembles lupus erythematosus so closely that the diagnosis can be made only by histologic examination. I think that it is the common flat type of lupus vulgaris, the feature of interest being the rather long duration.

DR. GEORGE M. MACKEE: I agree with Dr. Fox.

DR. PAUL E. BECHET: I also agree that the patch of lupus vulgaris is too deeply indurated to be classed as lupus vulgaris erythematodes (Leloir). I should rather cell it lupus vulgaris.

DR. J. FRANK FRASER: If I was asked to make a diagnosis in this case on the gross clinical appearance of the lesions, I should say it would rest between lupus erythematosus and lupus vulgaris. Of the two slides presented, one showed the picture of basal cell epithelioma. The other at one end showed a picture which could be interpreted as lupus erythematosus; at the other end the picture could be interpreted as lupus vulgaris.

DR. A. BENSON CANNON: Most of the patients from the New York City Hospital present one or more cutaneous conditions, as does the patient under discussion. I think the most interesting lesion in this patient is the one of lupus vulgaris which has remained localized on the cheek for so many years; it

resembles lupus erythematosus. The histologic picture was that of lupus vulgaris. The epithelioma on the right temple is clinically characteristic of basal cell epithelioma, as was also the histologic picture. It was thought that the patient's myocardial disease might be due to syphilis. The remarkable hardness, brownish discoloration, thickening and scaling of the skin of both legs suggested amyloid degeneration, but the patient was certain that this condition had been present only a few weeks, having followed a decided edema of the legs.

DR. FRED WEIDMAN (by invitation), Philadelphia: I agree with the histologic report that has been made of basal cell epithelioma in the one specimen and multiple miliary tubercles in the other one.

A Case for Diagnosis (Maculopapular Eruption on the Face). Presented by DR. FRED WISE.

W. J. G., a man aged 47, with an eruption on the cheeks for five years, was previously presented before the Manhattan Dermatologic Society, on Feb. 11, 1941 (ARCH. DERMAT. & SYPH., to be published).

DISCUSSION

DR. GEORGE M. MACKEE: I cannot make a clinical diagnosis. I examined the histologic slide but could not get the high power lens to operate satisfactorily. I cannot even suggest a diagnosis as a result of the histologic study. From what I did see in the slide, it seemed that there was a very substantial inflammation of a polymorphous type. I suspect, therefore, some form of granuloma.

DR. A. BENSON CANNON: I agree with Dr. MacKee about the histologic picture. I noticed considerable hemorrhage and some multinucleated cells. I think a more thorough and painstaking histologic study would probably solve the diagnosis.

DR. J. FRANK FRASER: I was unable to make either a clinical or a histologic diagnosis.

DR. JEROME KINGSBURY: Clinically, the lesions are not characteristic of any recognized dermatitis, and I am inclined to suspect that the condition is an artefact.

DR. HOWARD FOX: I agree with Dr. Kingsbury that a feigned eruption should be considered. Such a possibility is always in order in cases of this kind, in which the appearance is bizarre and in which no diagnosis can be made either clinically or histologically. Dr. Wise has not considered the stigmas of hysteria, though I do not know how much importance he attaches to them. The patient has an almost complete absence of the pharyngeal and corneal reflexes, and his personality might well be studied. He answered my questions in a rather pugnacious manner. I also suggest that tests for anesthesia be made.

DR. EDWARD R. MALONEY: I agree with Dr. Fox. In addition, here is an apparently healthy, intelligent person who has not worked for five years and who looks as though he ought to be able to get some kind of work to do.

DR. EUGENE F. TRAUB: I should like to ask the members who believe that this condition is a dermatitis artefacta how a man can produce a lesion that does not have any artificial contour. The patient's lesions appear to consist of small growths in the skin with a certain amount of pigmentation and are covered with almost normal epidermis. It seems impossible to me that any one could artificially produce such lesions.

DR. FRED WEIDMAN: As Dr. MacKee has said, there is a polymorphous infiltration and, as Dr. Cannon pointed out, some polymorphonuclear cells are present. There is also an arteritis. I think the condition is of endogenous origin, perhaps rheumatic. It could not possibly be dermatitis artefacta. It is a blood-borne process, I am sure, such as erythema elevatum diutinum, periarteritis nodosa and rheumatic nodules.

DR. FRED WISE: I reject the diagnosis of dermatitis artefacta in this case for the reasons which Dr. Traub mentioned and because of the lack of any visible evidences of changes in the epidermis such as would be made by cauterization or mechanical agents. The pathologists at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital were unable to offer a definite diagnosis.

A Case for Diagnosis (Localized Hyperpigmentation of the Skin and Eye). Presented by DR. HOWARD FOX.

W. L., aged 80, a retired merchant born in Austria, was referred from the Manhattan Eye, Ear, and Throat Hospital. About two and a half years ago he first noticed a brown spot, the size of a pinhead, near the right inner canthus. This has continued to enlarge, until at present it forms a square plaque with rounded borders, about 2¼ inches (6 cm.) in each dimension. The upper border is at the tarsal cartilage of the right lower lid. The patch is smooth except for a single tiny elevation in the central part. The color of the patch is not uniform, being deep brown in places and black in others. The borders are sharply demarcated and are not elevated. The skin of the rest of the face and the backs of the hands is unusually free from senile changes. There are no subjective symptoms.

On the sclera of the right eye, there are two ill defined areas, the size of a millet seed, of yellowish brown pigmention. One area is on the inner aspect and is roughly triangular, its base being at the limbus. The other patch is situated between the iris and the outer canthus.

The report of the ophthalmologist was as follows:

"There is sclerosis of the lens nuclei with numerous cortical opacities, greater on the left than on the right, and numerous vitreous floaters. There is no evidence of an intraocular mass or increased pigmentation. There are marked retinal arterioscleros.s and also slight melanotic pigmentation on the limbus. His vision with correction is 20/50 for each eye."

The lesion has never been treated. Urinalysis has shown the presence of sugar during the past month. The general health appears to be excellent.

DISCUSSION

DR. FRED WISE: My impression is that the lesion is a naevus pigmentosus tardus of nonmalignant character.

DR. GEORGE C. ANDREWS: I agree with Dr. Wise that this condition is essentially a nevus. In other words, I believe there are nevus cells in it. I disagree that it is entirely benign. It is a melanoma and may be fatal. The duration of two and one-half years, I imagine, covers both the nevus and the neoplasm. The growth has been spreading during that time, spreading enough to worry the patient and to bring him to a physician. I have seen a malignant growth of such a superficial type eventually invade the body and cause death. I believe the best treatment is to leave the lesion alone, on account of the patient's age. I do not believe any other treatment would be feasible.

DR. EUGENE F. TRAUB: Unfortunately, it is probably true that several different names might be correctly applied to such a lesion at this time, but I believe the one that would be accepted by the majority of dermatologists who have interested themselves in pigmentary processes would be lentigo maligna, which in fact combines the ideas expressed by Drs. Wise and Andrews. The term lentigo maligna in this connection does not necessarily refer to the size of the lesion at the time it is seen. The patient stated that the present lesion began as a pinpoint-sized spot and that it has grown rather rapidly to its present size in the past two and a half years. Therefore, if seen at the onset it would have been the size of a lentigo. The fact that the lesion has grown rather rapidly and that there has developed a certain amount of thickening in one portion, although the

major portion of it is still superficial, is evidence that the lesion is not an entirely innocent one. Such an idea, of course, is conveyed by the term lentigo maligna, which indicates that the lesion under discussion has malignant potentialities and might develop into a typical malignant melanoma. The term further indicates, however, that at present the pigmented mark is still relatively benign. If any type of treatment were undertaken, it would have to be a radical removal, which because of the age of this patient should not be considered.

DR. A. BENSON CANNON: I think that the patient has a malignant melanotic growth which in time will cause his death. The growth has already involved the greater portion of the lower lid, and in addition there is a wedge-shaped area on the conjunctiva just to the left margin of the pupil. I once observed a similar condition in a comparatively young woman which finally became so extensive as to necessitate a radical removal. This, however, was done too late to save her life. In all likelihood the growth in this man is a relatively slow one, and because of his advanced age I should think it would be unwise to interfere with it.

DR. J. FRANK FRASER: I should like to ask Dr. Fox if he noticed any pigmentation on the conjunctiva and whether it appeared at the same time as the lesion on the skin.

DR. HOWARD FOX: Yes, there is some pigmentation of the conjunctiva. I do not think the man knows whether that appeared at the same time as the original lesion on the skin.

DR. J. FRANK FRASER: From the appearance of the lesion I should say it is not malignant. Every once in a while one sees pigmentation on the conjunctiva or even on the eyeball which is benign. In regard to Dr. Andrews' suggestion that the condition is a nevus, the only way to determine that would be by histologic examination. If on such an examination no nevus cells were found, I should be inclined to call the lesion a benign melanosis. I think it is impossible for any one to determine from the gross appearance alone what the true nature of the process is. I advise a biopsy.

DR. R. H. RULISON: It seems to me that the only practical decision to be made in this case is how rapidly this condition is going to extend and how long the man is going to live. I advise against treatment.

DR. GEORGE M. MACKEE: The disturbing feature is the color of the pigment and the rapid evolution. So far as concerns the color, black is seen occasionally in basal cell epithelioma and in senile keratosis, and even in the common senile lentigo. However, I do not think the condition in this case falls into the same categories, partly because the eyeball and the conjunctiva are involved. It may be a nevus. However, my diagnosis is benign melanoma with malignant potentiality. Because of the man's advanced age, I advise against treatment. He should be kept under observation and treatment delayed until and if necessary.

DR. GEORGE C. ANDREWS: Before Dr. Fox closes I should like to discuss the term lentigo maligna mentioned by Dr. Traub. I do not like the term. It is confusing. It does not mean anything special because this condition is either a malignant melanoma or a naevus tardus. It is better to say that it is either a malignant melanoma or a pigmented nevus. In regard to Dr. Fraser's suggestion of a biopsy, I would be opposed to that on the grounds that obtaining a biopsy specimen would be a form of irritation.

DR. FRED WEIDMAN (by invitation), Philadelphia: The rapidity with which the condition spread would point more to a malignant melanoma. I have vividly in mind a patient presented before the Philadelphia Dermatological Society with a lesion which all the members thought was a melanoma and which turned out to be a pigmented basal cell cancer. In that case there was the black pigmentation seen in the melanoma interspersed with brown. I do not think that the black color would be inconsistent with a basal cell cancer. In our case the pigment had

been transported and lay deep in the corium in phagocytes. Whether it can pass on to the conjunctiva, of course, I do not know, but the possibility at least of a pigmented basal cell cancer should enter into the considerations here. As to the hazards of obtaining tissue for biopsy, I have not been deterred since I heard a presentation by Ewing at the Philadelphia Pathological Society a good many years ago. As I recall it, he had run three series of experiments with rats in mammary cancer. In one series he practiced massage; in another he cut biopsy specimens, while the third served as controls. He found that the incidence of metastasis was not greater in those in which biopsy specimens had been obtained than in the control group, but of course the incidence was higher in those which had been massaged.

DR. GEORGE M. MACKEE: I am glad to hear what Dr. Weidman said about biopsies. I think the dangers of obtaining biopsy specimens have been much overstressed. Some years ago I contacted nearly every cancer expert in the United States regarding this question, and the answer was always the same. If the tissue is carefully obtained, without any manipulation, such as massaging or squeezing, and if the wound is a clean scalpel cut or is properly made with the modern cutting current, there is no danger of metastasis. That holds true for any type of malignant lesion, including melanoma.

DR. EUGENE F. TRAUB: While I agree with Dr. Andrews that the term lentigo maligna has certain drawbacks, nevertheless, for a lesion of this character it is by far the best designation that can be used and is the one used in the official nomenclature. Certainly the term benign melanoma, in my opinion, is a far worse designation. Lentigo maligna is such a common and frequent lesion that it should be more generally recognized, and as it carries with it a definite prognosis, it at least has a specific meaning. It is the type of pigmentation that appears usually with advancing years, may grow rapidly and terminates frequently as a malignant melanoma. As I stated before, most of the dermatologists are well agreed on this term, which Becker and Obermayer thoroughly emphasized in their recent textbook (Becker, S. W., and Obermayer, M. E.: Modern Dermatology and Syphilology, Philadelphia, J. B. Lippincott Company, 1940) in the chapter on pigmentary disturbances. In the case of this patient, a man almost 80 years of age, a pigmentary spot like a freckle developed, which has grown rapidly and now exhibits malignant potentialties, typically the course of a lentigo maligna.

DR. GEORGE C. ANDREWS: Is not lentigo maligna always malignant?

DR. EUGENE F. TRAUB: A lentigo maligna is a pigmentary spot which begins small and not infrequently terminates as a malignant melanoma.

DR. HOWARD FOX: In view of the different opinions of the members, I no longer feel chagrined about my failure to make a diagnosis. I am still uncertain as to the nature of the disease and even how to name it. I agree that the danger of removing tissue for biopsy has been overrated, but I do not see the value of a biopsy in this case as no treatment is to be given. I agree with the opinion generally expressed, that in view of the patient's age and, I might add, the involvement of the eye, no treatment should be attempted.

A Case for Diagnosis (Lupus Erythematosus Disseminatus?). Presented by DR. FRED WISE.

A. G., a woman aged 39, was presented before this society on Jan. 28, 1941 (ARCH. DERMAT. & SYPH., this issue, p. 494). She has been in the hospital, very ill, with a high temperature, and the eruption has spread widely. A definite diagnosis has not yet been made.

DISCUSSION

DR. GEORGE M. MACKEE: I have seen the patient several times since her presentation and admission to the hospital. I still agree with Dr. Wise's original diagnosis of lupus erythematosus disseminatus. The woman is in a serious con-

dition. The eruption has become generalized. She failed to respond favorably to sulfanilamide. Recently she has received intramuscular injections of liver extract. She continued to get worse for several weeks, but recently there has been slight improvement.

A Case for Diagnosis (Sycosis Vulgaris in a Woman?). Presented by DR. EUGENE F. TRAUB.

S. S., a woman aged 40, was presented at a meeting of this society on Jan. 28, 1941 (ARCH. DERMAT. & SYPH., this issue, p. 506). On investigation is was found that pumice had definitely not been used. As I stated at the last meeting, she has done nothing but extract the hairs with tweezers. Neither electrolysis nor pumice stone had been used.

BROOKLYN DERMATOLOGICAL SOCIETY

SEYMOUR H. SILVERS, M.D., *President*

M. M. ESTRIN, M.D., *Secretary*

Feb. 17, 1941

Multiple Benign Cystic Epithelioma and Districhiasis. Presented by DR. C. THOMAS CHIARAMONTE and DR. C. B. LOCASTO (by invitation).

C. R., a 7½ year old boy, had peculiar "granules" on his lids which his mother first noticed while washing his face two years ago. Yellow mercuric oxide ointment and boric acid irrigations were employed, with no improvement. During the past three months the patient has been attending the ophthalmic clinic, where the lesions were scraped and expressed and silver nitrate was applied. The therapeutic procedure was of no permanent value, as the lesions subsequently recurred. There are no subjective symptoms.

The mother is married to a relative. The patient's maternal aunt, as a child, had a similar condition, which cleared up without any therapy. The patient has two sisters and one brother, all of whom are well.

The hairs growing along the edge of the upper eyelids are in double rows. In and about these hairs, and on the lower lids also, are numerous discrete and confluent, pinhead-sized, pearly, firm cystic masses. All other physical findings are normal.

Urinalysis showed no abnormality. The Wassermann reaction of the blood was negative. Examination of the blood showed 70 per cent hemoglobin, 3,400,000 red blood cells and 8,000 white blood cells.

DISCUSSION

DR. C. B. LOCASTO (by invitation): I called the condition in this case multiple benign cystic epithelioma because in cases of this disease (1) the onset is usually in childhood, (2) the lesions are pinhead-sized firm cystlike pearly masses, (3) there are no subjective manifestations and (4) there usually is a familial history.

DR. DAVID M. DAVIDSON: It is not always easy to make a clinical diagnosis of multiple benign cystic epithelioma, but in this case I do not believe that the diagnosis is correct. I believe the patient has merely filiform verrucae of the eyelids, as seen often in children. Even the diagnosis of districhiasis is doubtful, because I believe the verrucae themselves disturbed the growth of the hair and made it irregular.

DR. JOEL SCHWEIG: I agree with the last speaker that this case is one of filiform verrucae of the eyelids. The fact alone that the lesions have recurred

after removal by curetting makes a diagnosis of multiple benign cystic epithelioma improbable, since lesions of this disease do not recur on the same site after destruction.

Dr. Irving N. Holtzman (by invitation): Some of the histologic lesions of benign cystic epithelioma are definitely of appendage origin. I do not think the condition in this case is simple verruca. There is more than normal development of hairs in this boy's eyelids. As a rule there is only a single row of hairs. He has many more than the normal amount. Close inspection reveals several pinpoint-sized nodules adjacent to the margins of the lids. I do not want to call the condition benign cystic epithelioma without more recognizable lesions on the rest of the face. It may be a nevus in an unusual location.

Dr. C. Thomas Chiaramonte: I agree with the diagnosis of districhiasis because the child has a double row of hairs on both upper and lower lids. As far as the other diagnosis is concerned, I am inclined to disagree because the lesions are limited to the hair follicles, no other lesions are present and the lesions do not look like filiform verrucae to me; some look definitely cystic. I am inclined to agree with Dr. Holtzman that there is some nevoid element. Whether this is associated with districhiasis or not I am not able to say.

Dr. M. Edward Goebel: I understand that benign cystic epithelioma and trichoepithelioma are the same condition; both are classed as nevoid. They occur on the eyelids and not necessarily on the other parts of the face.

Dr. Abraham Walzer: I cannot see a possibility of these lesions being multiple benign cystic epithelioma. This disease is not very rare; it is seen rather infrequently, but I do not remember having ever seen lesions on the edges of the lids associated with lesions on the rest of the face which could be accepted as multiple benign cystic epithelioma. In this case the child has nothing but lesions on the edge of the eyelids, which alone clinically is not multiple benign cystic epithelioma. I think the whole process is blepharitis with some involvement of the hair glands, producing tiny cysts or possibly verruca.

Dr. C. B. Locasto (by invitation): In reference to districhiasis, the two rows of hairs have been present since infancy, that is, according to the mother. Therefore, the lesions which have been present for two years only are not the causative factor for the double row of hairs. The eyelids are lined by a stratified squamous epithelium, even at the lid margins. The basal cell layer is concerned with multiple benign cystic epithelioma, and where there are basal cells there is the possibility of multiple benign cystic epithelioma. In reference to blepharitis, no inflammation of the lid margins is present.

Hereditary Hemorrhagic Telangiectasia. Presented by Dr. Max Dickman.

C. S., a white man aged 41, is presented from the Red-Hook Gowanus Health Center, Brooklyn. He complains of frequent epistaxis, bleeding from his face when shaving or rubbing with a towel and bleeding from his lips especially when eating. The eruption has been present for at least thirty years. He states that he does not know whether any other member of his family has a similar condition.

On the ears, cheeks, chin and nose are numerous dark red telangiectases, spider-like telangiectases and a few red punctate raised pinhead-sized angiomas. On both lips, but mainly on the lower, are about twenty-five red punctate raised angiomatous lesions. There are a few lesions on the palate and on the sides of the tongue.

DISCUSSION

(The members were in unanimous agreement with the diagnosis as presented.)

Filiform Fibroma and Verrucae of the Face and Chin. Presented by Dr. Seymour H. Silvers.

R. B., a married Negro aged 23, complained four weeks ago of sores of the face and chin of one year's duration. The eruption began on the chin. More

lesions appeared later when an attempt was made to remove the lesions by the "electric needle."

One year ago he had pleurisy.

Examination shows numerous pinhead-sized to lentil-sized, skin-colored, well defined raised, elongated lesions above the surface of the skin.

The Wassermann reaction of the blood was negative.

During the past three weeks he has received 600 r of unfiltered roentgen rays.

DISCUSSION

DR. C. THOMAS CHIARAMONTE: I think the patient has verruca plana juvenilis. Some of the lesions are a little bit higher than those ordinarily found in verruca juvenilis, but many of them are flat and shiny.

DR. JACOB SKEER: I agree with the diagnosis. I find the condition difficult to treat and cure. I have used a bismuth compound, roentgen rays and endothermy, with poor results. In 1 case, a married woman aged 22 had lesions on the face for eighteen months. All of the aforementioned therapy was used without any apparent success. Her condition was cleared up after two injections of neoarsphenamine (0.4 Gm.).

Tuberculosis of the Skin. Type? Presented by DR. M. EDWARD GOEBEL.

G. C., a 27 year old Negro, was admitted to the surgical ward two months ago for the first time because of pain in both legs. After a two weeks' course of rest in bed, he was discharged to the dermatologic clinic, where a diagnosis of erythema induratum was suggested.

The patient was admitted to the dermatologic service one month ago with the same complaint of painful legs. For five years tender small nodules had been appearing on the hands, arms and legs. These would as a rule break down and discharge pus. Some have been ½ inch (1.3 cm.) beneath the skin. For the past few months they have been appearing more rapidly. A node has been present behind the angle of the right mandible for five months.

Examination reveals hyperpigmented areas on the hands arms, legs and feet, several small tender subcutaneous nodules, a few small punched-out ulcers, a large node at the angle of the right mandible and a few small nodules on the external ear.

A Mantoux test with a 1:1,000,000 dilution elicited a pustular reaction at the site of injection. A histologic section suggested a Darier-Roussy sarcoid structure. A roentgenogram of the chest failed to show pulmonary tuberculosis. The Wassermann reaction of the blood was negative. The white blood cell count was elevated above normal.

DISCUSSION

DR. M. EDWARD GOEBEL: I saw the patient last week for the first time. He was at Kings County Hospital two months ago, where the injection of a 1:1,000,000 dilution of tuberculin elicited positive reaction. The nodes are extremely tender. Some of them break down and discharge pus.

DR. H. L. FEIGENBAUM: The condition looks like erythema induratum (Bazin's disease). The fact that the reaction to a tuberculin test was so strongly positive that necrosis followed is highly suggestive of true tuberculosis of the skin.

DR. ABRAHAM WALZER: I cannot see why tuberculosis of the skin should be considered in this case at all. One is apt to jump to conclusions because of the positive reaction to a tuberculin test. Because the reaction was positive does it follow that any lesions he might have must be tuberculous? The lesions impress one as some type of pustular folliculitis, not tuberculosis. The lesions are not typically tuberculous clinically, and I doubt whether they will show any tuberculosis on histologic section. My diagnosis is that of simple folliculitis.

DR. DAVID M. DAVIDSON: I completely disagree with the diagnosis of folliculitis; neither folliculitis nor any other pyogenic infection produces nodular lesions which remain for weeks and then liquefy, ulcerate and leave scars. The only

pyogenic infection that may produce nodules which ulcerate is furunculosis, and the conditon in this case certainly is not furunculosis. The lesions, although not typical, are probably an expression of erythema induratum. Boeck's sarcoid and Darier-Roussy sarcoid can be excluded on clinical grounds alone; they do not liquefy or ulcerate.

DR. C. THOMAS CHIARAMONTE: The biopsy revealed in the subcutaneous fatty layer a diffuse infiltration of epithelioid cells and, as far as I could see, one giant cell. There was no definite tubercle formation. One important point concerning this patient is the fact that coincidentally with these lesions on the arms and legs there is an enlarged gland on the right side of the neck. On the helix of the right ear there are numerous nodules. These small nodules and occasional ulcerated areas are suggestive of papulonecrotic tuberculid, but the histologic picture does not bear out such a diagnosis. In my opinion, the patient has tuberculosis of the skin, but I cannot put his lesions into one definite class.

DR. DAVID M. DAVIDSON: It was mentioned that the pathologic study revealed a structure of sarcoid. It is sometimes difficult to make a differential diagnosis between some of the sarcoids and erythema induratum, especially the Darier-Roussy type. If the lesions of erythema induratum have not reached the stage of necrosis, the only differential point would be the amount of lymphocytic infiltration present.

DR. L. J. FRANK: I saw the patient when he first entered the hospital. At that time he had large nodules on the lower extremities which were slightly painful.

DR. M. EDWARD GOEBEL: I happened to see the man after the active lesions had subsided. My understanding is that sarcoid is usually not painful. This man described his lesions as very painful. As a rule they do not break down. I understand that at one time these nodules broke down and discharged material. Erythema induratum may break down and be painful, but it usually occurs on the calves of the legs and in women. It is best to call the condition tuberculosis cutis rather than to attempt to follow a narrow classification.

Multiple Idiopathic Hemorrhagic Sarcoma. Presented by DR. SEYMOUR H. SILVERS.

T. B., a man aged 22, consulted me ten weeks ago about a "ringworm" infection of the toes for which he had received treatment for two years. Questioning elicited the statement that he had been suffering from "tonsillitis" for the same length of time. During childhood he had been treated for more than one year for congenital syphilis. He has three brothers and two sisters, who are apparently normal. The father and mother are living. The father's blood still gives a positive Wassermann reaction.

Examination at the first visit showed a malodorous fungating mass of the toes of the right foot and raised red pigmented marble-sized tumors on the dorsum of the foot and on the right hand. There was an ulcerating egg-sized mass on the right tonsil. The Wassermann reaction of the blood was negative.

A histologic section of an early lesion of the foot confirmed the diagnosis of Kaposi's sarcoma.

With roentgen ray therapy, the lesions of the right toes and hand improved, and the fungating mass healed.

The patient was sent to the Memorial Hospital for the Treatment of Cancer and Allied Diseases for radium therapy to the tonsillar area. The diagnosis was confirmed after additional histologic studies, and the tonsillar lesion was removed surgically.

There is at present a smooth raised area at the right tonsillar fossa. Complete opening of the mouth is difficult.

DISCUSSION

DR. C. B. LOCASTO (by invitation): I saw the patient when he had lesions on the dorsa of the feet and maceration between the toes. The lesions were purplish

and infiltrated. What impressed me most was the lesion on the right tonsil, because it looked identical with the lesions on the feet except that it was covered by a mucous surface. The disease is in a relatively young man and is supposed to have started when he was about 14.

DR. JOEL SCHWEIG: It is a known fact that Kaposi's sarcoma may appear at an early age. I have under observation a woman who has had for the past twenty-five years extensive Kaposi's sarcoma which appeared in her youth and has progressively involved all the extremities and the face. In the last few years sarcomatous lesions have developed on the hands, which yielded to radium treatment. No metastases have developed to date.

DR. L. CHARGIN: Kaposi's sarcoma can occur in the very young. I saw a child of 6 months with this disease. It can appear at any age. The disease runs a short or a long course. It attacks the skin of the mucous membranes, or it may attack the viscera. Sometimes it is very acute, but more often it is chronic. I know of a case in which the condition was present for fifteen years; and there are many other cases of longer duration. It is just one of those diseases about which little is known.

DR. ABRAHAM WALZER: I should like to point out that in too many cases Kaposi's sarcoma ends in sarcoma or some other form of lymphoblastoma. There probably is a definite relation between Kaposi's sarcoma and the lymphoblastomas.

Knuckle Pads. Presented by DR. ABRAHAM WALZER.

L. P., a man aged 53, a Chinese, is presented from the Brooklyn Jewish Hospital. There is nothing in his past history of any significance. Though employed as a cook now, his cutaneous lesions developed while he was employed as a gardener about nine months ago.

There are lesions on the backs of the joints of both hands. On the right hand the digits and joints involved are: the thumb, the interphalangeal joint; the second, third and fourth fingers, the proximal interphalangeal joints, and the fifth finger, both interphalangeal joints. On the left hand, the digits and joints involved are: the thumb, the interphalangeal joint; the second finger, all three joints with the process extending from the base of the finger to the wrist in band formation; the third and fourth fingers, the proximal interphalangeal joints, and the fifth finger, both interphalangeal joints.

The lesions in these areas consist of elevated, indurated, sharply outlined erythematous patches, about the size of a dime. The normal markings of the skin are exaggerated, and they are covered with a faint scale. They are freely movable over the underlying structures.

Histologic examination of a section taken from the patch on the back of the hand showed the following features: The epidermis showed decided hyperplasia. The stratum corneum was about ten times its normal thickness, and the granular layer was about five cell layers in thickness. The papillae were elongated and showed mild dilatation of the blood vessels, with a scant perivascular round cell infiltration.

Knuckle Pads. Presented by DR. ABRAHAM WALZER.

J. B., a Negro aged 16, presented from the Brooklyn Jewish Hospital, was the oldest of six children. The second oldest, a boy aged 10, died in 1936 of pulmonary tuberculosis. At that time an examination of the patient revealed some evidence of tuberculosis of the nodes at the hilus. A Mantoux test with a dilution of 1:10,000 elicited a 3 plus reaction. Subsequent roentgen examinations of the chest showed the process to be healing.

The condition of the patient's hands has been present for about five years. His father incriminates a habit of biting and sucking the back of his finger joints as the cause for the condition. The lesions are on the backs of the joints of

both hands. They include the interphalangeal joints of both thumbs, all the metacarpophalangeal joints except those of the fifth fingers and all the proximal interphalangeal joints.

The lesions are dime sized, sharply outlined, elevated and flat. The surface is somewhat hyperkeratotic. The skin is adherent but the lesions move freely over the underlying bone. The color of the lesions is much lighter than that of the adjacent skin.

The histologic picture was practically the same as that in the preceding case.

DISCUSSION OF TWO CASES OF KNUCKLE PADS

DR. JACOB SKEER: This condition is supposed to follow trauma of various types. Knuckle pads always occur on the proximal interphalangeal joints and rarely on the distal joints, as in this boy. There is proliferation of connective tissue in the cutis and subcutis.

DR. H. L. FEIGENBAUM: A milder form of knuckle pads is fairly common. I have seen the condition in several children who do a good deal of marble playing and whose knuckles come in contact with the rough sidewalk, but cases in which the lesions are so striking, such as those presented tonight, are not common.

DR. SEYMOUR H. SILVERS: There was some thickening of the skin over the knuckles extending to the dorsum of the hand. The skin showed marked lichenification. There was no fatty part or pad underneath the lichenified skin.

DR. DAVID M. DAVIDSON: Knuckle pads may sometimes be confused with erythema elevatum diutinum (Bury's disease). About a year ago I presented a case before this society with the diagnosis of erythema elevatum diutinum, but the pathologic diagnosis reported later was heloderma. There are two types of knuckle pads: a type for which one finds a traumatic factor as the cause, as seen in lumbermen, gardeners and card players, and a type with which one does not find any etiologic factor, the so-called idiopathic condition. The condition in the cases presented tonight probably belong to the first type. The histologic structure is usually that of hyperplasia of the epidermis.

DR. JOEL SCHWEIG: While I agree with the diagnosis in the Chinese, I believe that the eruption of the Negro belongs to a different classification. The Chinese has a typical appearance of knuckle pads, described under various other names, such as heloderma of Vorner, which is usually of a traumatic origin. The Negro's condition I would classify as a nevus, most likely of congenital origin. The lesions are not indurated; they are rather thickened with pronounced markings, reminding one of cutis verticis gyrata of the scalp.

DR. IRVING N. HOLTZMAN: I think the condition is simply some manifestation of epidermal hyperplasia of the skin as a result of physical stimuli. The histologic structure in the 2 cases is identical. One could not tell one slide from another. The changes are limited exclusively to the epidermis. The mild inflammatory changes in the corium are secondary to the physical or chemical effect of the thickened skin.

DR. ABRAHAM WALZER: The name knuckle pads is permissible. In Sutton and Sutton (Diseases of the Skin, ed. 10, St. Louis, C. V. Mosby Company, 1939, p. 650) there is a picture of this condition under this title. Knuckle pads, therefore, are not a new condition, but they are not seen often. They are not altogether an occupational condition, because they sometimes occur in persons whose occupation does not account for them. Knuckle pads have been connected with Dupuytren's contractions. They are also associated with contracture of one of the fingers. All these conditions probably have some hereditary basis; they are not altogether due to injury. On the other hand, in some instances direct connection between trauma and this condition exists. It is interesting to note that in all the cases of knuckle pads that have been reported, it has never been seen on the thumbs. Both the

patients presented have affected thumbs. It has also been said that involvement of the distal interphalangeal joint is rare. These patients have the condition on this site. The therapy in cases of this kind is unsatisfactory.

A Case for Diagnosis (Dermatitis Herpetiformis?). Presented by DR. JACOB SKEER.

J. M., a married white American man aged 39, came to the dermatologic clinic of the Brooklyn Jewish Hospital complaining of a generalized eruption of fifteen months' duration.

The patient stated that he had been taking ex-lax and that his child had had an eczematous eruption for more than a year. In July 1940 he had numerous lesions on the arms and legs, which had a tendency to ring formation, with clearing centers. The lesions on the margins were excoriated, and there was decided pigmentation.

Present examination reveals patches of pigmentation of various sizes and dug-out excoriated lesions, as well as atrophic scars, on the anterior and posterior surfaces of the thighs, legs, arms and forearms. There are sharply defined areas of erythema, lichenoid papules covered with scales and hyperkeratosis on the dorsa of the hands and fingers. There are deep fissures on the knuckles.

The reaction to a Kline test was negative. Urinalysis gave normal results on several occasions. Examination of the blood revealed a hemoglobin of 65 per cent, 3,000,000 red blood cells and 8,000 white blood cells, with 48 per cent polymorphonuclear leukocytes, 1 per cent segmented cells, 49 per cent lymphocytes and 2 per cent eosinophils.

Histologic examination showed that the epidermis was thinned with slight parakeratosis in scattered areas. The granular layer was not prominent. The stratum germinativum showed irregular finger-like acanthosis. The papillae were hypertrophied and showed vascular dilatation. There was a slight cellular reaction, chiefly perivascular, of round cells and fixed connective tissue cells. In one area the cellular infiltrate extended throughout a papilla, thinning out the overlying epidermis and giving the impression of a subepidermal bulla. The vessels in the deeper layers of the skin showed some inflammatory reaction of a similar nature, but not as great. The diagnosis was a chronic inflammatory process.

A mycologic examination showed no fungi.

DISCUSSION

DR. DAVID M. DAVIDSON: A few tentative diagnoses were offered when this patient was presented for the first time at the clinical conference of the dermatologic clinic. Among these were dermatitis herpetiformis and fungous infection. Dermatitis herpetiformis had to be taken seriously into consideration in view of the fact that the patient presents three of the cardinal features of that disease: grouping, pigmentation and atrophy. The pigmentation, however, is mostly of the macular type and not of the type usually seen in that disease. The patches themselves are clear in the center and active at the borders, which are sharply marginated. The last two features make me prefer the diagnosis of fungous infection. I do not think that much consideration need be given to the fact that an examination for tinea gave no results, because it was done only once and that was after the patient had used various local applications.

DR. C. THOMAS CHIARAMONTE: There is a definite history of tinea of the feet. I did not examine his feet, but the patient states that his toes are itchy. The lesions appear to be an eczematous type of dermatophytid. Against the diagnosis of dermatitis herpetiformis are an absence of brownish pigmentation and failure to find lesions at the points subject to pressure. One would expect to see lesions around the shoulders and hips. As far as fungi are concerned, in only exceptional instances can fungi be found in the scrapings from such lesions.

DR. L. J. FRANK: Why consider the case as one of dermatitis herpetiformis? I could not see any suggestion of lesions in the definite areas of pressure. I do not think the pigmentation was the kind one would see in dermatitis herpetiformis. I received an impression of an eczematoid condition, caused possibly by some external irritant.

DR. JOEL SCHWEIG: A Trichophyton purpureum infection is to be considered in cases of typical and atypical dermatitis herpetiformis. I wish to recall the case Dr. Tolmach and I published (Generalized Trichophyton Purpureum Infection Simulating Dermatits Herpetiformis, ARCH. DERMAT. & SYPH. **41**:732-735 [April] 1940), which was also presented before the New York Academy of Medicine, Section of Dermatology and Syphilis. The diagnosis made by the majority of the members was one of dermatitis herpetiformis, while the condition actually was a case of tinea due to T. purpureum. I suggest a culture for fungi in this case and also a therapeutic test in the form of application of compound ointment of benzoic acid N. F., which ought to clear the patch within forty-eight hours if the underlying condition is a fungous infection.

DR. JACOB SKEER: The fact that the man may have had dermatophytosis of the feet does not rule out dermatitis herpetiformis.

A Case for Diagnosis (Lupus Erythematosus with a Toxic Dermatosis?).
Presented by DR. M. EDWARD GOEBEL.

C. D., a man aged 50, married, noticed fifteen years ago a rash on his right cheek. He was treated for about four years and received injections of a gold compound. A biopsy was performed at the time, and a diagnosis of lupus erythematosus was made. At this time he was seen by me. On his right cheek over the zygomatic process was an area of atrophy, and on the border of this atrophic area were numerous vesicles. At the dermatologic clinic of the Post-Graduate Medical School and Hospital a histologic examination showed lupus erythematosus with bullous lesions. He received many injections of a gold compound, and the condition cleared up. However, during the past ten years there have been slight recurrences, which responded well to a few injections of a gold preparation. In July 1939 considerable vesiculation occurred on the right cheek, and he received a bismuth compound intramuscularly and sulfanilamide by mouth. While he was under this regimen, the rash spread over his entire face, upper extremities, chest and lower extremities. On August 22 a biopsy specimen was taken. The pathologic report suggested vesicular iodide eruption. He received sodium arsenate intramuscularly without any improvement, and as he gradually became worse, he was hospitalized in October. During his stay in the hospital he had an elevated temperature with each fresh outbreak and was acutely ill. Four weeks ago the rash reappeared.

Examination shows the atrophic area on the right cheek as noted in 1930. There is a symmetric distribution on the face, upper extremities, chest and lower extremities of erythematous, vesicular and crusted areas. There is no pigmentation or atrophy.

DISCUSSION

DR. C. THOMAS CHIARAMONTE: I am inclined to believe that the condition is some type of erythema multiforme because the patient has remissions and recurrences and the lesions are symmetric.

DR. JACOB SKEER: I am inclined to believe that this condition is a bullous type of lupus erythematosus or a Senear-Usher type of pemphigus. The patient has seborrheic lesions. He has a seborrhea-like erythema of the face, as well as vesicular lesions, which have not all cleared up. Those that are seen tonight have erythematous bases. Ormsby calls a disease like this pemphigus erythematodes. There are vesicles, atrophic scars and erythema. The man certainly had lupus erythematosus; so I think his condition is the Senear-Usher syndrome.

DR. L. CHARGIN: The condition is neither the Senear-Usher syndrome nor lupus erythematosus. It is a form of a toxic eruption. It might be a new clinical entity. I have observed 2 or 3 cases of this condition. There is an atrophic patch, usually on the side of the forehead, with bullae at the borders. In former days this condition was called a limited type of pemphigus. It ran a slow course and acute pemphigus never developed, from which patients died. Later on when lupus erythematosus of the bullous variety was reported and described the two types were confused. The condition in this case is neither one nor the other. It is some kind of toxic eruption, the nature of which I do not know.

DR. M. EDWARD GOEBEL: I believe the patient had lupus erythematosus at first and later a bullous type of erythema multiforme developed. I believe the cause of both conditions is toxic in origin; there are two lesions produced by a toxic disturbance, one presenting itself as lupus erythematosus and the other as erythema multiforme. Cases of this kind have been described. The Senear-Usher syndrome is a pemphigus eruption, while the other condition is not; it is rather a benign type of lupus erythematosus.

SEYMOUR H. SILVERS, M.D., *President*

M. M. ESTRIN, M.D., *Secretary*

March 17, 1941

Lichen Sclerosus et Atrophicus. Presented by DR. JACOB SKEER.

F. R., a white woman aged 63, a widow, born in Russia, reported to the Brooklyn Jewish Hospital on March 5, 1941, complaining of itching of the vulva and of the anal region.

The patient had dermatophytosis of the feet in 1930 and varicose dermatitis of the left leg in 1932. In 1939 there was a sharply defined erythematous eruption in the vulva and groins of two months' duration. The impression was tinea with contact dermatitis due to phenolated petrolatum. In May 1939 there was a recurrence. In July 1939 the patient complained of severe itching. In June 1940 there were sharply defined erythematous lesions in both groins, with scaling and itching. On March 5, 1941 the patient complained of recurrence of itching of the vulva of several weeks' duration.

In the groin are seen discrete, irregular, oval and round, pearly white atrophic spots which are slightly depressed below the level of the skin and vary in size from that of a pinhead to that of a pea.

Examination of the vulva shows redness and atrophy of the vaginal mucosa. The posterior portions of the labia are reddened, covered with white macerated epidermis and superficially fissured.

On the flexor surfaces of the wrists there are white discrete atrophic lesions with some sclerosis.

Examination of the blood showed normal sugar, urea and uric acid content. The cholesterol and phosphorus values of the blood were within normal limits. The sedimentation rate was 24 mm. in sixty minutes. The white blood cell count was 10,900, and the differential ratio was within normal limits.

DISCUSSION

DR. L. FRUCHTBAUM: This case is peculiar in that the lesions on the forearms and around the vulva differ somewhat in appearance. Those on the wrists appear to me to be white, raised, flat-topped lesions, whereas those on the inner aspects of the thigh look more atrophic. The picture is more that of lichen albus than

that of lichen sclerosus et atrophicus. In the latter condition the lesions remain stationary or get worse and never disappear. In this case the appearance and distribution of the lesions are so characteristic as to make me favor the diagnosis of lichen albus.

DR. D. M. DAVIDSON: In answer to the previous speaker, this patient presents characteristic lesions of lichen sclerosus et atrophicus. This disease begins with slightly elevated white polygonal papules, and one can see such lesions on the patient's wrist. As the disease progresses and the atrophic stage sets in, the papules become white atrophic spots; such lesions are present on the patient's vulva. The sites of predilection for this disease are the chest, shoulders and back, but it may appear on and around the vulva.

DR. JOEL SCHWEIG: I agree with the diagnosis as presented. In the presentation there was left out a description of the lesion appearing in the right lower quadrant of the abdomen. This lesion is of the size of a silver dollar and has a smooth, elevated, indurated border and a violaceous halo. This lesion by itself would put the dermatosis into the class of morphea, since it has all of the characteristics of this disease, but considering the case as a whole, I believe the condition belongs in the class of lichen sclerosus et atrophicus and constitutes the end stage of the process. The lesions on the vulva possess all the characteristics, with the exception of the follicular plugs, which are regularly but not necessarily seen in cases of this disease. The case is instructive, since such an extensive involvement of the vulva is rare.

DR. M. E. GOEBEL: I did not see all the lesions. The one on the vulva impressed me as being one of morphea.

DR. A. WALZER: The whole question of white lichen lesions has been very much discussed and still is the subject of controversy. At present the trend is to disregard the term white spot disease. Lichen albus, as reported by von Zumbusch, is regarded not as a type of lichen planus but as a definite entity. At present the tendency is to group these white lichen lesions into three types: lichen sclerosus et atrophicus, morphea and lichen planus with atrophy. If a lesion in the course of its development shows a stage of lichen planus, it is lichen planus atrophicus; but if it does not, it is put under the heading of lichen sclerosus et atrophicus. Morphea guttata is not lichen and has been often called white spot disease. Histologically and clinically, therefore, a definite distinction can be made between these three types. This particular patient shows two stages: the early stage of white lichen papules on the wrists and the later stage of atrophy around the vulva. Histologically, the lesions do not show the picture of lichen planus.

A Case for Diagnosis (Rupioid Psoriasis? Chronic Lichenified Eczema?).
Presented by DR. H. L. FEIGENBAUM.

E. K., a Negress aged 24, divorced, has one child 5 years of age, whose Wassermann reaction was negative. She presented herself at the dermatologic clinic of the Kings County Hospital in January 1941 with a lesion on the left elbow. This lesion, the patient claimed, had been present continuously for the previous twelve years. It is supposed to have followed trauma. It becomes traumatized easily because of its location and because of the patient's occupation, which is that of a domestic. It bleeds occasionally and is covered with crusts and heavy scales most of the time.

The lesion is roughly oval and about 3 by 2 inches (7.5 by 5 cm.) in size. It is situated dorsally over the elbow joint. It is sharply demarcated, infiltrated and lichenified. Part of it is covered with heavy scales and crusts. It is not painful or pruritic. It is composed of conglomerating individual papular lesions, especially noticeable around the border.

The Wassermann reaction of the blood on February 1 was 4 plus.

Histologic examination showed changes in both the epidermis and the corium. The epidermis showed edema, both intracellular and intercellular. There were decided parakeratosis and hyperkeratosis and an almost total absence of the stratum granulosum. Acanthosis was only moderate. The corium showed round cell infiltration with occasional plasma cells and some blood vessel proliferation. Some of the vessels showed round cell infiltration especially in the upper part of the corium.

The patient has had four injections of a bismuth compound plus potassium iodide, administered orally, from February 8 to date, without any change in the lesion.

Roentgenograms of the elbow and lungs were normal.

DISCUSSION

DR. I. J. FRANK: I should hesitate to call one single patch in a Negress psoriasis. In my opinion her condition is neurodermatitis. The lesion is sharply outlined with oozing, scaling and crusting. It did not impress me as being tuberculosis, for I did not see any nodules.

DR. M. L. WEITZ: I feel that, as Dr. Frank just said, it is difficult to label one patch as psoriasis. With a positive Wassermann reaction, despite the fact that there has not been any apparent improvement after four injections of a bismuth compound and the administration of potassium iodide by mouth, I feel that one should consider the possibility of a psoriasiform syphilid.

DR. C. T. CHIARAMONTE: When one looks at the elbow casually one sees a psoriasiform type of lesion; it has well defined borders and a psoriasiform crust. On closer inspection, the lesion is evidently made up of rather large papules, many of which are capped with a crust. Histologically, the presenter states that there are intracellular and intercellular edema and parakeratotic scales. Correlating the clinical and the pathologic observations, one would narrow the differential diagnosis down to syphilis, tuberculosis and, possibly, a bromide eruption. The presence of a perivascular round cell and plasma cell infiltrate and some thickening of the blood vessels would favor the diagnosis of tertiary syphilis, with psoriasiform crusting. Tuberculosis may be readily eliminated by the histologic picture.

DR. A. WALZER: When one slide does not give any information, I think other sections should be made and studied. In this case the histologic studies do not help. Therapeutic results will show whether the lesion is syphilitic or not. I think syphilis, tuberculosis or a bromide eruption are the best suggestions offered.

DR. L. FRUCHTBAUM: How long can a syphilitic lesion persist without causing some atrophy? In this case there is a history of twelve years' duration without such evidence. The fact that the patient has syphilis is no reason to ascribe any lesion she may have to syphilis. Aside from the histologic report, which is the only factor to be guided by, there is the clinical picture: the verrucous nodules, the duration of the disease and the lack of symptoms. Everything points to tuberculosis verrucosa cutis.

DR. M. E. GOEBEL: It is true that psoriasis in Negroes is very uncommon, but it has been seen. I know of two or three dermatologists here who have seen it. In fact, at one time the idea was advanced to treat patients with psoriasis with intramuscular injections of Negro blood, but this idea was discarded because several cases of psoriasis were observed in Negroes.

DR. M. SILVERMAN: I have seen several tertiary nodules of syphilis which have persisted for years without destruction and have disappeared after treatment without leaving scars. I do not think it necessary for every tertiary syphilid to leave ulceration and atrophy.

DR. E. A. GAUVAIN: In every case of psoriasis in a Negro at Kings County Hospital—and there have not been very many—there has always been the story of white blood mixture. I do not believe it was ever found in a full-blooded Negro.

DR. JACOB SKEER: Dr. Howard Fox presented several cases of psoriasis in full-blooded Negroes (*J. Cutan. Dis.* **34**:847, 1916).

DR. A. WALZER: I suppose that any rule in medicine can have an exception. Generally speaking, psoriasis in the Negro does not occur.

DR. H. L. FEIGENBAUM: First of all, I thought of syphilis and tuberculosis, but a biopsy showed no trace of tuberculosis of the skin. As far as syphilis is concerned, I could not see how a syphilitic lesion could be of twelve years' duration without atrophy or other changes. I was loathe to accept the diagnosis of psoriasis because of the rarity of this condition in Negroes and also because there was only one patch. As to chronic lichenified eczema, it is possible that the lesion was being kept up by continuous trauma. Histologically I do not think one can definitely say that the condition is psoriasis, as chronic lichenified eczema might produce a similar picture.

A Case for Diagnosis (Dermatitis Factitia?). Presented by DR. D. M. DAVIDSON.

J. P., a 36 year old Negress, born in the United States, is presented from the Jewish Hospital of Brooklyn.

The present eruption began six months ago as a boil which was not very painful. After a week's duration, the patient opened the boil, squeezed out a lot of pus and applied iodine liberally. After three weeks, she consulted a private physician, who told her to apply olive oil.

At present the patient has a quarter-sized erythematous patch on the left cheek which is slightly elevated, has sharply marginated irregular arciform borders, is infiltrated and is covered with pitted scars, plugs and a small thin crust; the scars and plugs are darker in color than the rest of the lesion. A few pitted scars and comedos are scattered over both cheeks.

The Wassermann reaction of the blood was negative.

Histologic examination revealed nonspecific chronic perifollicular inflammation.

DISCUSSION

DR. C. T. CHIARAMONTE: Not having seen the slides, I should like to inquire whether or not the basal cell layer was broken up anywhere. I also should like to know about the appearance of the collagen fibers. Clinically, the lesion impresses me as lupus erythematosus; there is a well defined patch on one cheek with depressions and elevations, follicular plugging and a scaly border.

DR. M. SILVERMAN: What little I saw, without feeling the border, makes me think the condition is lupus vulgaris rather than lupus erythematosus. The histologic picture sometimes is not specific.

DR. JACOB SKEER: I have had the opportunity of watching this patient, and I am still at a loss to make a definite diagnosis. The lesions that I first saw were covered with crusts and grease, and on removal of the debris the lesion appeared to be evenly reticulated; whether this was due to the plaques or the pinpoint-sized necrotic lesions I do not know. She gave a history of rubbing oil and iodine on that lesion for several weeks or months. Probably the condition might be a foreign body reaction.

DR. M. E. GOEBEL: I think the description given by Dr. Chiaramonte is that of lupus erythematosus, and clinically that is my diagnosis.

DR. JOEL SCHWEIG: From the clinical standpoint alone, the diagnosis of lupus erythematosus should be considered. The additional facts in the history, as given by Dr. Skeer, such as rubbing of oil by the patient into the lesion for several weeks, recall experiences I had in Europe during the World War. Owing to the shortage of refined and purified petrolatum, the ointment bases consisted of crude oils which produced severe reactions of the skin in sensitive persons, especially on the face.

These reactions were named vaselinoderma. It is possible that the condition in this case may belong to the group of dermatitis venenata due to hypersensitiveness to liquid petrolatum.

DR. A. WALZER: When this patient first came to the clinic the lesion was raised and boggy. My first impression was lupus vulgaris. As a matter of fact, by means of a toothpick, I thought I demonstrated the apple jelly nodules. Then, with some mild local therapy, the lesion regressed considerably. At present it does not look like either lupus erythematosus or lupus vulgaris—at least, it is not typical.

DR. S. H. SILVERS: I suggest that, if possible, more tissue for biopsy be taken and that serial sections be made, because if the condition should be lupus vulgaris, changes are often seen in different parts of the skin. This is especially true if the specimen for biopsy is obtained from the central portion of the lesion and not from around the periphery.

DR. D. M. DAVIDSON: When the patient was first seen at a clinical conference two diagnoses were offered by the dermatologists present: lupus vulgaris and lupus erythematosus. A biopsy was performed, and the histologic picture did not confirm the clinical impression. The pathologic study of the slides revealed a decided hyperkeratosis of the horny layer with plugging and a slight acanthosis with an enlarged granular layer under some of the plugs. The corium was the seat of an inflammatory process with perifollicular cellular infiltration as the main feature. The infiltration consisted of round cells, few polymorphonuclear leukocytes and a number of fibroblasts, clumped in places. The elastic tissue was normal. In view of the clinical impression, as mentioned, and the altogether different histologic picture in this case, I find it difficult to make any definite diagnosis.

MINNESOTA DERMATOLOGICAL SOCIETY

CARL W. LAYMON, M.D., *President*

F. W. LYNCH, M.D., *Secretary*

Minneapolis, Feb. 22, 1941

Erythroderma. Presented by DR. H. E. MICHELSON, Minneapolis.

O. G., a white man aged 49, a printer, was in good health until the summer of 1933. At that time he was caught in a sudden squall while in a small boat. He made shore after an experience which he said caused him great fright. He noticed that within a few minutes after he landed his skin became red and extremely pruritic. This conditon has existed practically unchanged. Altogether he has spent over a year in the hospital since that time and has had numerous types of therapy, including hypnosis.

The patient appears well developed and well nourished. The entire skin is erythematous and indurated. On the abdomen the involvement is at present papular, while that of the extremities is nodular. There is some scaling, particularly on the hands and feet. The nails are rough and greatly thickened.

Smears of blood and skin taken for microscopic examination showed no evidences of lymphoblastoma. He has at times had a mild leukocytosis, but all the cells have been mature.

(Histologic sections were shown.)

Erythroderma. Presented by DR. H. E. MICHELSON, Minneapolis.

J. T., aged 33, an employee in a milk plant, noticed two small red nonpruritic plaques in the inguinal region in January 1940. The lesions remained unchanged until June, when four more similar patches appeared in each inguinal region and

one over each biceps muscle. The lesions spread rapidly, and by August the entire body was involved and the skin had become extremely pruritic.

He was admitted to the University Hospitals on October 4. The skin gradually improved under generalized treatment with wet packs, followed by the application of 3 per cent salicylic acid in petrolatum; however, during his hospitalization mental symptoms developed. He was discharged on Jan. 14, 1941 but was readmitted on February 15.

The skin is red and covered with a rather coarse, easily detachable scale. There is oozing in some of the folds. The scalp is covered with fine hair, which is growing in after a complete alopecia. The finger nails are thickened, have transverse ridges and are worn flush with the ends of the fingers. Some of the toe nails have been shed. Those remaining are thickened and rough and show a tendency to split.

Smears of the blood and bone marrow as well as histologic sections of the skin showed no evidences of lymphoblastoma.

(Histologic sections were shown.)

DISCUSSION OF CASES OF ERYTHRODERMA

Dr. J. R. Webster (by invitation), Chicago: I am interested in these 2 cases of erythroderma because I have had a case that is similar, under observation clinically and histologically for about eight months, and there has been little improvement, if any. My patient began to have trouble on the hands and arms when he was working with cement, and the diagnosis was originally made elsewhere of cement worker's dermatitis. However, it began to spread until eventually he had a generalized erythroderma. His blood count showed about 16 per cent eosinophils several times, but otherwise there were no changes in the blood. His lymph gland system did not seem to be clinically involved. Histologically, as far as the skin was concerned, there were variation in size and staining qualities of the infiltrating cells and slight pyknosis and karyorrhexis, enough to suggest that the condition might be an unusual form of mycosis fungoides. I therefore tried to use small doses of roentgen rays on some localized areas, with no result. Along with that and continuing for some time thereafter, I administered sodium cacodylate intravenously, with slight improvement. The condition in this case apparently began as a dermatitis due to an external irritant and eventuating in this type of picture, with some suggestions of belonging in the lymphoblastoma group but not exactly fitting in there as far as the response to therapy was concerned. My conclusion was that the condition was based on a sensitization dermatitis.

Dr. Hamilton Montgomery, Rochester: The condition in the first case histologically shows practically all the features of psoriasis. There are many features to suggest this diagnosis clinically. In fact, the case is comparable to one at the Mayo Clinic at present, a case of generalized psoriasis with pustules.

The histologic changes in the second case would fit in with a neurodermatitis or atopic eczema, but histologic distinction from early mycosis fungoides is difficult because there are few immature white blood cells and some clumping of the cells and the infiltrate is rather dense. Some conditions of this kind remain essentially as atopic dermatitis, whereas others eventuate in one of the lymphoblastomas. This type of condition is the most difficult to diagnose either clinically or histologically. It is my impression that the disease in the second case, however, is a generalized neurodermatitis or an atopic eczema.

Dr. H. E. Michelson, Minneapolis: I want to call attention to the fact that patients with long-standing generalized dermatoses frequently have profound psychic disturbances. I do not believe this has been taken into consideration enough in the past. In institutions where psychiatric management is available it should be used in conjunction with dermatologic treatment.

Parapsoriasis. Presented by Dr. H. G. Irvine and Dr. D. D. Tunnacliff, Minneapolis.

A man aged 43 first noticed a few lesions on the flexor surface of the right arm three years ago. Since then new lesions have developed on the other arm, the body and the legs. He states that since the eruption appeared there has been no change in the size of the lesions and that none has disappeared. The eruption does not itch.

On the flexor surfaces of the upper part of each arm are round fawn-colored lesions with dry adherent scales, from 1 to 2 cm. in diameter. On the body and on the upper parts of the thighs all of the lesions are symmetrically distributed and elongated in the lines of cleavage. Some of the older lesions are atrophic.

(Histologic sections were shown.)

DISCUSSION

Dr. O. H. Foerster (by invitation), Milwaukee: The patient showed several interesting features which usually are not part of the classic picture of parapsoriasis. A patient with a similar condition, that is, slowly progressive, with the eruptive lesions in linear striations and along the lines of cleavage and with only slight infiltration and scaling and no subjective symptoms, was seen with Dr. Arndt of Berlin in 1914, when he was visiting in this country. Dr. Arndt confirmed the diagnosis of parapsoriasis, of the plaque type of scaly erythroderma of Brocq. I have seen the patient occasionally since then and observed that the lesions have remained practically unchanged and that there has been no further extension.

In contrast to this stationary and mild variant of parapsoriasis en plaques there are cases in which pruritus is a prominent feature and in some of these the condition eventually turns out to be mycosis fungoides. I have observed such instances and have learned that cases presumably of érythrodermie pityriasique en plaques disseminées of Brocq in which the condition is actively inflammatory or pruritic to any decided degree should always be suspected of being cases of mycosis fungoides masquerading under this clinical picture in the prefungoid stage.

Dr. Michelson remarked that dermatologists in this country are perhaps more prone to make a diagnosis of parapsoriasis than are the dermatologists abroad. I agree that the diagnosis is not always as well substantiated as it should be. However, I think a fairly large number of cases are observed that are true instances of two of the three forms in which parapsoriasis presents itself. The guttate form is one of these, including the varicella-like acute type of pityriasis lichenoides chronica of Juliusberg, cases of which have been presented repeatedly and described more especially by Senear and Oliver.

The second form is characterized by the presence of scaling disseminated plaques and is the form of parapsoriasis with which dermatologists are well acquainted, for it is more frequently encountered. I believe it is particularly this form that presents itself often as a variant, does not adhere closely to the classic concept of parapsoriasis en plaques and may occur in only partly developed types, of which I think the condition in the patient shown today is an example.

As to the third and extremely rare form—known as parapsoriasis lichenoides of Brocq and lichen variegatus of Crocker, Fox and McLeod and originally described as parakeratosis variegata by Unna, Santi and Pollitzer—there are only about 15 proved cases in the literature, with only a few in this country. It is interesting to know that in several of the group originally observed by Unna the condition was later found to have terminated as mycosis fungoides, and this is of importance in view of the similar termination observed in cases of parapsoriasis en plaques, as previously described.

Dr. M. Oppenheim (by invitation), Chicago: In several respects the efflorescences simulate the picture of purpura annularis telangiectodes (Majocchi's disease); other eruptions do not have such telangiectasia and ring and oval forms with a pale center. I was surprised to see in this case the efflorescences follow the lines of cleavage, a condition one often sees in parapsoriasis. I am not able

to make a definite diagnosis; I did not see the histologic sections. I think this condition belongs to the large group of parapsoriasis, which includes so many different cutaneous diseases of which nothing at all is known except the clinical and histologic observations.

A Case for Diagnosis (Lupus Erythematosus?). Presented by DR. FRANCIS W. LYNCH, St. Paul.

I. W., a man aged 23, a university student, noticed an eruption on the abdomen in the spring of 1938. By the spring of 1939 the chest was involved, first on the sternum and then laterally. Not until 1940 did the patient notice that his cheeks were redder than the rest of his face. The lesions on the face have not spread except for one new plaque over the left zygoma. The lesions have caused no subjective symptoms but seem to sunburn much more readily than do the uninvolved areas of skin.

There are two poorly circumscribed erythematous lesions on the cheeks. There are slight telangiectasia, dilatation of the follicles and a small amount of fine scaling. A similar area is present over the left zygoma. On the anterior surface of the trunk is a symmetric eruption made up of plaques on the medial portion of the chest, along the midline and laterally on the chest and abdomen. Each plaque is made up of a large number of pale red papules. Pressure eliminates most of the erythema.

The white blood cell count has always been within normal limits. The reaction to a Mantoux test was positive, but roentgenograms of the chest showed no pathologic changes. There has been no albumin in the urine at any time.

DISCUSSION

DR. MAURICE REUTER (by invitation), Milwaukee: This case is unusual. There is not a great deal to see clinically. I was surprised in looking at the slide with Dr. Montgomery to see the microscopic picture of xeroderma pigmentosum. In other words, there were epidermal atrophy, irregular proliferation of the rete pegs and at their ends proliferations of the basal cells, forming bulblike or clublike ends, with some inflammatory reaction in the cutis. Xeroderma pigmentosum seems like a far-fetched diagnosis, but I do not know of any other disease that will produce that microscopic picture. I suppose the old argument comes up: Which will be accepted, the clinical or the microscopic observations? I offer the diagnosis of xeroderma pigmentosum without pigment.

DR. HAMILTON MONTGOMERY, Rochester: Clinically, Dr. Lynch's patient shows no plugging and little atrophy or other features of lupus erythematosus. A histologic section of tissue from the abdomen shows all the characteristic features of xeroderma pigmentosum and duplicates the histologic changes in a patient whose case Dr. Reuter and I reported (Xeroderma Pigmentosum, ARCH. DERMAT. & SYPH. **26**:256-257 [Aug.] 1932). The lesions on the abdomen in our patient also paralleled the clinical appearance of the nonpigmented papules on the abdomen in this patient. The specimen for biopsy from the face of Dr. Lynch's patient is very small and again shows no evidence of lupus erythematosus. It simply shows the picture of a toxic erythema. On the other hand, there is no evidence of proliferation of the rete ridges with broad tips to the rete ridges resulting from proliferation of the basal cells, which, when considered with atrophy, telangiectasia and a mild perivascular infiltrate, is characteristic of xeroderma pigmentosum. One might call the condition in Dr. Lynch's case, therefore, xeroderma pigmentosum without pigmentation. The patient is sensitive to light, and there are cases in which xeroderma pigmentosum develops late in life. It is not necessary to have epithelioma develop. The patient whose case Dr. Reuter and I reported is living and well and has very little pigmentation, simply by avoiding the sun and by using cosmetics. Dr. Lynch's patient remembers that several members of his family had freckles but does not remember of any having cutaneous cancers.

I recently saw a woman in her forties with a mild xeroderma pigmentosum, typical clinically as well as histologically, who had one cancer removed from the lip but otherwise has had no trouble; she takes care not to go out in the sun unless she wears a large-brimmed hat. Her brother has a similar condition and has had several cutaneous cancers removed.

DR. H. R. FOERSTER (by invitation), Milwaukee: Before hearing the discussion on this interesting case, I was inclined to look on the condition as an unusual manifestation of chronic toxic erythema, possibly precipitated by sensitization to light. I wonder if that interpretation can still be entertained.

DR. H. E. MICHELSON, Minneapolis: I should like to ask Dr. Montgomery what he predicts for the patient. Dr. Lynch has demonstrated the patient before a group at the University on several occasions. I proposed a diagnosis of a nevoid condition at one time, but if Dr. Montgomery and Dr. Reuter make a diagnosis of xeroderma pigmentosum, then the prognosis certainly should be guarded.

DR. HAMILTON MONTGOMERY, Rochester: Answering Dr. Michelson's question regarding prognosis, I believe there is nothing to be concerned about if the patient protects himself from the sun. In xeroderma pigmentosum there are a hereditary tendency and a definite history of light sensitivity. There is a peculiar but distinctive type of histologic change that could be regarded as a nevoid disturbance, in the broad sense of the word. Therefore, because there is no typical xeroderma pigmentosum of the face in this case, one could equally well regard the condition as an unusual type of epithelial nevus. I believe another specimen for biopsy should be taken from the face, as the one taken simply showed a picture of toxic erythema. The pathologic changes in the lesion from the abdomen are much different from those seen in eczema on a light sensitivity basis.

Scleroderma. Presented by DR. J. F. MADDEN, St. Paul.

Mrs. J. G., a white woman aged 50, stated she first noticed that white spots appeared on the breasts in 1939. The lesions were accompanied by itching.

Examination shows atrophic plaques covering the entire ventral surface of both breasts and the skin of the chest between the breasts. There are also isolated white atrophic maculopapules extending to the anterior surfaces of the breasts. There are similar maculopapules involving the perineum, vulva and perianal region. The vulva appears to be atrophic.

The Wassermann reaction of the blood was negative.

Circumscribed Scleroderma. Presented by DR. H. E. MICHELSON, Minneapolis.

M. A. D., a white girl aged 12 years, had on the right shoulder an area which became darker and stiffer than the rest of the skin in September 1938. Since then new lesions have appeared on the back, on the face and on the right side of the chest. The patient was told by her family physician that she had "leakage of the heart." There was no history of rheumatic fever, chorea, tonsillitis or other acute infections at any time in her life except for mild scarlet fever at 3 years of age.

When she was first seen there was a bandlike area running from the right shoulder down the flexor surface to the palm. The involved skin was indurated and lighter than normal. On the chest, on the right breast and on the lower part of the back were patches which were regarded as circumscribed scleroderma. The basal metabolic rate in March 1939 was 0 and —4 per cent. Examination of the blood showed 78 per cent hemoglobin; the white blood cell count was 6,900 per cubic millimeter, and the differential count was within normal limits. In May 1938 the urine showed slight reactions for albumin.

At present there is a somewhat atrophic area extending from the right scapula down the inner surface of the arm to the palm. The pigment is mottled. The underlying muscles are slightly atrophic.

(A histologic section was shown.)

DISCUSSION OF CASES OF SCLERODERMA

DR. MARCUS R. CARO (by invitation), Chicago: I think that in both cases the diagnosis of scleroderma has been established both clinically and histologically. In the young girl, of great interest to me was the linear distribution of the lesions. Dr. Senear and I recently (Lichen Striatus, ARCH. DERMAT. & SYPH. **43**:116 [Jan.] 1941) reviewed the literature in an attempt to find some theory that would explain the linear distribution of all linear dermatoses, including lichen striatus, linear scleroderma, linear psoriasis, linear lichen planus and linear nevi. Any theory that explained the distribution of one would do just as well for the others. The various theories that have been proposed include the distribution of lesions along the cutaneous blood vessels and lymphatics, the lines of cleavage of the skin, the lines of junction of the dermatomeres and also Voigt's lines, that is, the boundary lines separating the zones of distribution of cutaneous nerves. According to a more recent theory, a person is born with certain fragile zones, or zones of increased reactivity, due to some embryologic change, which will determine the localization of lesions in later dermatoses. In the cases we reported we could find no one theory to explain the distribution of lesions. I think that in the present case of linear scleroderma the distribution is zosteriform and that it probably follows the distribution of a dorsal root ganglion.

A Case for Diagnosis (Balanitis Xerotica Obliterans?). Presented by DR. J. F. MADDEN, St. Paul.

J. H., a white man aged 65, stated that the posterior half of the urethral meatus became white and hard about December 1939. At this time a painless bean-sized white papule developed on the glans penis to the right of the frenum and smaller similar papules on the prepuce and other portions of the glans penis. The papule near the frenum grew slowly but steadily, while most of the others have disappeared. In February 1937 the patient presented himself at the genitourinary disease clinic complaining of difficulty in starting urination and of multiple streams of urine. He stated that he had had difficulty starting urination during the previous five years. A stricture was found, and there was a large bean-sized periurethral abscess. The patient was circumcised in infancy. The Wassermann reaction of the blood was negative. Gonococci were not found.

DISCUSSION

DR. M. OPPENHEIM (by invitation), Chicago: This case is one of atrophic change of the penis with a stricture of the orificium in which the question arises whether the condition is kraurosis penis, erythroplasia of Queyrat or leukoplakia. All these questions are difficult to answer because they concern a disease which is very rare; I observed only a few cases in Vienna. The condition is the same in kraurosis vulvae. I class such conditions in the group of dermatitis atrophicans, because the histologic process is first inflammation and later degeneration of the elastic fibers.

Early diagnosis in such cases is difficult. Itching is an important subjective symptom in these cases of kraurosis penis, as in cases of kraurosis vulvae, and another important diagnostic factor is the age of the patient. Kraurosis vulvae appears after the climacterium; kraurosis penis is mostly known in older men—in the "climacterium" of men. Yesterday I saw a younger man in Dr. Michelson's clinic with a probable erythroplasia, who had different symptoms. There is no doubt that one has to differentiate erythroplasia, xerosis penis, leukoplakia penis and induratio plastica of the corpus cavernosum glandis penis. The condition in this case, I believe, is induratio plastica penis. A stricture of the orificium is present without doubt, and on palpation of the corpus cavernosum penis et urethrae one feels induration. The patient stated that when the penis is in erection it is not straight but curved and bent. Through the glans penis and around the orificium an induration is felt. Another important sign for this diagnosis is that the patient

has a Dupuytren contracture. This symptom is often observed with induratio plastica penis. The stricture of the urethra is due to the shrinking of the connective tissue in the corpus cavernosum glandis.

Hereditary Hemorrhagic Telangiectasia. Presented by DR. J. F. MADDEN, St. Paul.

J. B., a laborer aged 56, stated that telangiectases first appeared on his face about 1910. New lesions have appeared at intervals; old lesions have enlarged, but none has disappeared. At present the skin of the face, neck and upper part of the trunk, the mucous membranes of the mouth and the nasal septum are involved. There are also telangiectases in the conjunctiva. The patient has had nosebleeds as often as two or three times a day since childhood. In 1929 he was treated for what was thought to be a hemorrhagic duodenal ulcer. The patient's father has had repeated nosebleeds throughout his life. Studies of the blood, including determinations of the bleeding time and clotting time, fragility tests and a platelet count, gave results which were within normal limits.

DISCUSSION

DR. F. T. BECKER, Duluth: I agree with the diagnosis as presented. It might be mentioned that a similar condition is also seen associated with cirrhosis of the liver. I recently saw a 9 year old girl who had numerous lesions which I thought were hereditary hemorrhagic telangiectasia. However, on further examination it turned out that she had cirrhosis of the liver. This should be kept in mind; sometimes a dermatologist may be able to make a diagnosis of systemic disease rather early in its course.

DR. ROBERT R. KIERLAND, Rochester: The point that Dr. Becker brought out in regard to the association of hereditary hemorrhagic telangiectasia with cirrhosis and other conditions of the liver is a point not generally recognized by dermatologists. Osler made the statement that angiomas have curious relations with infections of the liver. Williams and Snell (Pulsating Angioma [Generalized Telangiectasia] of the Skin Associated with Hepatic Disease, *Arch. Int. Med.* **62**:872-882 [Nov.] 1938) have recently brought out the relation of pulsating angioma and hereditary hemorrhagic telangiectasia to various forms of hepatic disease, including cirrhosis, metastatic carcinoma, hepatosplenomegaly and even familial types of cirrhosis.

Sarcoid. Presented by DR. H. E. MICHELSON, Minneapolis.

Mrs. J. P., aged 67, noticed red spots on her arms in 1937. Similar spots have since appeared on her entire body. There have been no subjective symptoms. Albuminuria was found, and there was moderate anemia, but the leukocyte count was normal. The results of serologic tests for syphilis were negative. The sedimentation rate was 115 mm. in one hour. Roentgen ray studies of the bones and lungs showed typical changes of sarcoid.

There were in 1938 numerous red-brown to dark brown spots covering the entire body. These spots were superficial and freely movable. Many of the lesions have healed with atrophy. The edge of the liver is palpable 2 fingerbreadths below the costal margin. Sections of the skin and of the tonsils show histologic changes consistent with a diagnosis of sarcoid. All the lesions have healed.

(Histologic sections were shown.)

Sarcoid of Boeck. Presented by DR. S. E. SWEITZER, Minneapolis.

Mrs. E. K., a white housewife aged 45, first noticed a pimple on the dorsum of the right forearm in 1933. This pimple became a plaque, which grew rapidly peripherally, healing in the center, until 1936, when it was 4.8 by 3.7 cm. Since then its spread has been slower.

On the dorsal and lateral surfaces of the right forearm is an annular lesion 8.5 by 5.5 cm. with a brownish red border about 7.5 mm. in width and with areas of scaling. The center of the lesion is depressed and white with prominent follicles and fine hairs. The epidermis appears atrophic and has a ringed arrangement. The serologic reaction was negative. The reaction to a Mantoux test with a 1:100 dilution of tuberculin was negative. Tuberculin, 1:20, in hydrous wool fat rubbed into the lesion elicited no reaction. In 1937 a course of treatment with potassium iodide, four injections of a bismuth compound and twelve injections of neoarsphenamine did not have any influence on the lesion. In April 1940 a roentgenogram of the fingers and toes was normal, and one of the thorax showed a Ghon tubercle, calcified mediastinal glands and infiltration of both lungs consistent with a diagnosis of sarcoid of Boeck. Histologic examination showed changes characteristic of sarcoid of Boeck.

Recent therapy has included solid carbon dioxide, the application of which to the active border under moderate pressure for thirty seconds on Nov. 15, 1940 has apparently arrested peripheral spread of the lesion.

DISCUSSION OF CASES OF SARCOID

DR. H. F. FOERSTER (by invitation), Milwaukee: Both of these cases are interesting, though there is no question about the diagnosis, the histologic picture being typical of sarcoid in each. I do not recall having seen the follicular atrophy with peripheral concentric extension exhibited by the patient with the solitary lesion of the forearm, and in this case the response to treatment with solid carbon dioxide is noteworthy. The photographs of the pronounced eruption in the other woman explain the extensive scarring now present. The customary inclination to accept all examples of sarcoid of Boeck as having a tuberculous cause and the frequent clinical similarity of lesions of this disease to those of definite types of cutaneous tuberculosis warrant emphasizing the possibility of a nontuberculous cause. Persistently negative reactions to tuberculin tests may be accepted as evidence of anergy or hypoergy to tuberculosis and also as indicating the possibility of absence of tuberculosis, while the typical histologic picture of sarcoid differs much from that of cutaneous tuberculosis. Also the roentgenographic observation of nontuberculous fibrosis in the lungs, with absence of a history of tuberculosis or clinical manifestations of the disease, and the cystic osseous changes in Boeck's sarcoid seem to place some of these conditions in a group that may be regarded as having a definitely nontuberculous causation.

Circumscribed Myxedema. Presented by DR. H. E. MICHELSON, Minneapolis.

Mrs. L. G., a white housewife aged 57, was operated on in June 1940 for thyrotoxicosis. About a year ago she noticed a small mass on the anterolateral surface of the lower part of the right leg just above the ankle. This mass has increased rapidly in size during the past year and is now about 10 by 15 cm. It is painless except for throbbing when she is on her feet for a prolonged period, when it becomes swollen and red. A similar lesion appeared on the left leg shortly after the appearance of the one on the right. This second lesion followed a similar course.

On the lateral surfaces of the lower parts of the legs are poorly defined areas of thickened brawny induration, and the skin covering them shows dilated follicles, so that it resembles pigskin.

The basal metabolic rate in June 1940 was +44 per cent; in November it was +6 per cent, and on Feb. 8, 1941 it was +17 per cent.

(Histologic sections were shown.)

DISCUSSION

DR. ROBERT R. KIERLAND, Rochester: The classic case of localized myxedema is the type of case presented, in which the lower outer third of each shin is

involved. Although a condition of this kind is usually seen in association with recurrent exophthalmic goiter, it is not generally recognized that it may occur in association with primary exophthalmic goiter and in about 25 or 30 per cent of the cases. Lesions of localized myxedema may be found anywhere on the skin.

A Case for Diagnosis (Scrotal Tongue?). Presented by Dr. H. E. Michelson, Minneapolis.

R. M., a 57 year old superintendent of schools, has had a scrotal tongue all his life. In May 1940 he noticed bleeding from the gums. Then white spots appeared on his lip and later on the tongue.

On his tongue and on the lips are pinhead-sized white papules. The mucous membrane appears red and edematous.

DISCUSSION

Dr. F. T. Becker, Duluth: For the past year I have been much interested in various avitaminoses and their relations to the skin. In my opinion this man has a typical scrotal tongue. The inflammatory reaction of the tongue (glossitis), the cheilitis and also the perlèche have been described as due to a riboflavin deficiency. I believe the patient should have a determination of vitamin B in his blood made and should be given fairly large doses of vitamin B complex, especially riboflavin. He eats very little meat, and his diet has been restricted as far as food containing vitamins of this nature is concerned.

Dr. M. Oppenheim (by invitation), Chicago: There is no argument with the diagnosis in cases of aphthous stomatitis. Only what is new to me is the little white nodule below the tongue and the condition of the face. I never encountered such a case in Vienna. In normal times there was no vitamin B deficiency, but during and particularly after the World War I published reports of cases in Vienna and Austria under the name pellagroid, a condition resulting from poor nutrition and corn bread. In the cases of pellagroid I did not see oral lesions, but the soldiers with pellagra, who came from the Italian battlefields, had typical lesions of the oral mucous membrane. In cases of pellagroid only the cutaneous symptoms of the pellagra triad were present and, as oral lesions, depapillation of the tongue and gingivitis. After my publication of the Viennese cases, pellagroid was found in Berlin, Tirol and other places.

Dr. J. F. Madden, St. Paul: Dr. Daly, of Tufts Dental College, had an extensive exhibit on oral lesions at the meeting of the American Medical Association in New York in 1940. He showed several patients who had cardiorenal disease accompanied by an increased content of the blood urea due to the irritation of ammonia eliminated in the mouth. These conditions were more common in patients who had artificial dentures but were also seen in other patients. I think it would be worth while to determine the urea content of the blood in this case.

Necrobiosis Lipoidica Diabeticorum. Presented by Dr. H. E. Michelson, Minneapolis.

Mrs. M. B., aged 38, first noticed a red spot on the lateral surface of the right leg in 1937. This area increased in size, and in 1938 two similar spots, which also increased in size, appeared nearby. Shortly thereafter two similar spots appeared on the left leg. In 1940 she noticed a similar lesion on the lower part of the left side of the abdomen. The large lesion on the left leg has been discharging pus for some time and is painful.

The patient is obese. There are three lesions on the right leg, the largest of which is 8 by 5 cm., with pustular depressions and irregular borders. The color is deep purple. On the left leg are two lesions, 3 by 4 cm. and 3 by 3 cm. On the lower part of the abdomen is a lesion 2.5 by 3.5 cm. These smaller lesions vary from reddish violet to reddish brown.

The fasting blood sugar level was elevated, and a dextrose tolerance test showed a typical diabetic curve. There has repeatedly been sugar in the urine.

(Histologic sections were shown.)

Necrobiosis Lipoidica Diabeticorum. Presented by DR. S. E. SWEITZER, Minneapolis.

A. L., a white woman aged 19, who had had diabetes mellitus for many years, noticed a red spot in the middle of her legs during the summer of 1935 after she fell down a flight of stairs and injured her legs. She was first seen in the outpatient department of the Minneapolis General Hospital on Aug. 15, 1935, and a biopsy specimen was taken. She stated that after the specimen was taken the lesions started to grow until 1939, when they reached their present size.

The patient is well developed and has on her right leg an hourglass-shaped yellowish red plaque, 5 to 2 inches (13 to 5 cm.) in size. On her left leg is a round plaque 1½ inches (4 cm.) in diameter. Her diabetes is now controlled with 70 units of protamine zinc insulin daily.

(Histologic sections were shown.)

Necrobiosis Lipoidica Diabeticorum. Presented by DR. S. E. SWEITZER, Minneapolis.

N. H., a white woman aged 64, had a condition diagnosed as diabetes mellitus in 1930. She noticed a spot developing on her right leg in 1936, when it was the size of a cent. At that time she was seen at the Minneapolis General Hospital, outpatient department, and a biopsy specimen was taken. After this, the patient stated, the lesion grew for three years, until it reached the present size. A similar lesion began on her left leg in 1935 but disappeared within two months without local treatment. One sister died of diabetes.

The patient is well developed. On the lower third of the right leg she has a yellowish red plaque of irregular outline, measuring 5 by 4.7 cm.

(Histologic sections were shown.)

Nondiabetic Necrobiosis. Presented by DR. S. E. SWEITZER, Minneapolis.

Mrs. L. R., a white woman aged 56, was first seen in the Minneapolis General Hospital, outpatient department, on June 30, 1934 and gave the history that in 1925 she first noticed a lesion on her right leg which she thought was a bruise. However, it did not disappear and has persisted and changed to its present color. Subsequently similar lesions appeared on the right knee and on the lower part of the right leg. The lesion on the knee disappeared spontaneously two years ago. In 1937 two lesions appeared on the left leg. Her mother died of diabetes mellitus.

On both lower extremities several depressed yellowish firm irregular plaques are present. A Mantoux test with a dilution of 1:10,000 of tuberculin in 1934 and in 1941 resulted in a 4 plus reaction. Roentgenograms of the chest and bones were normal. Blood sugar on several occasions was normal. Tests of the urine showed no sugar. A sugar tolerance test on Feb. 18, 1941 showed the following results: 105 mg. per hundred cubic centimeters while the patient was fasting, 190 mg. after one-half hour, 175 mg. after one hour, 130 mg. after two hours and 110 mg. after three hours.

(Histologic sections were shown.)

Granuloma Annulare. Presented by DR. S. E. SWEITZER, Minneapolis.

B. D., a white girl aged 11 years, was first seen at the Minneapolis General Hospital, outpatient department, on Jan. 15, 1941. She has noted for the past three months ringlike lesions which appeared first on the left knee and then on the left ankle, left calf and left elbow, and the most recent lesion, within the last

two weeks, appeared on the right ankle. She had a severe burn at the age of 1 year, which involved the face, forearms and hands.

The patient is a normally well developed child whose skin shows severe scarring resulting from a burn. Annular lesions, from 1 to 3.5 cm. in diameter, are seen on the left knee, ankle, calf and elbow and on the right ankle. The result of a Mantoux test with a 1:10,000 dilution of tuberculin was negative. Biopsy confirmed the diagnosis.

DISCUSSION OF NECROBIOSIS AND GRANULOMA ANNULARE

DR. M. OPPENHEIM (by invitation), Chicago: I should like to talk about dermatitis atrophicans lipoidica. Montgomery, Hildebrand and Rynearson of the Mayo Clinic reported on this disease with a review of 78 cases since my first publication. Eight cases were reported from the Mayo Clinic. It is a surprise to me to find so many cases of this disease in this country, for instance 4 typical cases at this meeting. In the Austrian, French, Italian and German literature are only a few cases. In the last German publication, by Boldt (*Arch. f. Dermat. u. Syph.* **179**:74 [May] 1939), is a very good summary of 35 cases of this disease besides his own 16 cases. In 14 per cent of the cases no diabetes could be found. In Chicago I observed 3 cases in the Cook County Hospital in the service of Drs. Ebert and Cornbleet. The patients were women; in all there were lesions on the legs. Two had diabetes, and 1 did not have it. I asked the latter about her family history. She told me that her father and mother had died of diabetes. One of the 4 patients presented here did not have diabetes, but her mother had died of it. I am of the opinion that the condition in all these cases, which are typical instances of dermatitis atrophicans lipoidica—I do not use the name necrobiosis lipoidica; I use the name dermatitis atrophicans diabetica, which I gave to this disease in my first paper in 1929—has something to do with sugar metabolism and the fat and cholesterol metabolism. The factor of heredity in these cases is significant.

I consider the clinical picture of the cutaneous diseases more important than the results of laboratory examinations; for me the skin is the litmus paper of the organ. I think that when cases of dermatitis lipoidica atrophicans diabetica are encountered without diabetes, the family history should be investigated, or other marks of a disturbed fat or sugar metabolism should be looked for. I believe that one will find other symptoms and also a family history of the disease.

With regard to the clinical symptoms, I have always felt that there is confusion. The clinical picture is well defined, with three or, in some cases, four stages (*Arch. f. Dermat. u. Syph.* **166**:576, 1932). It starts with a sharply limited round hard red papule; this papule grows at the periphery and becomes depressed in the center, forming a ring. The center is yellow and the periphery red (second stage). The yellow center becomes depressed; telangiectasia appears, and the skin is tense and atrophic (third, atrophic, stage). Finally in some of these efflorescences round sharply defined ulcerations appear, usually covered by a crust (fourth, necrotic, stage). My histologic observations, which were proved by all investigators, such as Dr. Montgomery, show perivascular round cell infiltration and thickening of the blood vessels, homogenization and degeneration of the collagenous fibers, degeneration and absence of the elastic fibers, lipoid deposits in the tissue and possibly degeneration of the connective tissue and elastic fibers.

I do not believe that collagen can be changed to fat, but I believe that degenerated connective tissue and elastic fibers can be substituted by fat and that small fat droplets follow the course of the connective tissue fibers. The thick lipoid drops which are stained reddish brown by sudan III are in the necrotic center of the lesions, but small and numerous droplets follow the course of the collagen fibers. Therefore, Kreibich was not so wrong when he described a lipoid degeneration of the collagen.

I believe that dermatitis atrophicans lipoidica diabetica is the correct name for this interesting new cutaneous disease, because, as in acrodermatitis atrophicans,

an inflammation is followed by a degeneration of the collagen and elastic fibers. I should not confuse this disease with granuloma annulare. The two diseases are totally different clinically and histologically. The cause of granuloma annulare is not known, but the cause of dermatitis atrophicans lipoidica diabetica is known.

DR. FRANCES C. PRUNTY (by invitation), Rochester: I was especially interested in noting the association of the case of granuloma annulare with the 4 cases of necrobiosis lipoidica diabeticorum, including 1 without diabetes. Bernstein (Necrobiosis Lipoidica Diabeticorum [Urbach], ARCH. DERMAT. & SYPH. **36**:282 [Aug.] 1937) pointed out the histologic similarity of the two conditions. He stated that in certain instances it was necessary to have positive sudan III stains for fat in order to differentiate necrobiosis lipoidica diabeticorum from granuloma annulare. I have recently reviewed 30 cases of granuloma annulare observed at the Mayo Clinic, in 12 of which I studied the biopsy material. While I believe there are other definite points of differentiation between the two conditions, namely, the definite vessel changes and the extent and arrangement of the infiltrate in necrobiosis lipoidica diabeticorum, the histologic similarity is frequently decided. I also found positive staining for mucin in all cases of granuloma annulare but not in those of necrobiosis lipoidica diabeticorum. The case of granuloma annulare was typical both clinically and histologically. In my recent review I found nothing which I thought suggested tuberculosis as an etiologic factor in granuloma annulare. The infiltrate of epithelioid cells, lymphocytes and fibroblasts in a radial arrangement around an area of myxomatous degeneration, not caseation necrosis, does not present the picture of true tubercle formation. The changes in the vessel walls and the association of the tubercle formation with vessels, as seen in the hematogenous types of tuberculosis, are not seen in granuloma annulare.

DR. HAMILTON MONTGOMERY, Rochester: I agree with what Dr. Oppenheim has said, including the statement that necrobiosis is not a good term; yet, like sarcoid, it has survived through prolonged and common usage. Dr. Prunty was discussing the histologic similarity between granuloma annulare and necrobiosis. Clinically, differentiation between the two conditions is readily made.

Dr. Hildebrand, Dr. Rynearson and I pointed out that in 90 per cent of the cases of necrobiosis lipoidica diabeticorum the patients are women and in 90 per cent the patients are diabetic (Hildebrand, A. G.; Montgomery, H., and Rynearson, E. H.: Necrobiosis Lipoidica Diabeticorum, *Arch. Int. Med.* **66**:851 [Oct.] 1940). However, in 18 per cent cutaneous lesions preceded the onset of the diabetes by a period of a few months to several years. This simply reenforces Dr. Oppenheim's concept that possibly every patient with this disease is potentially diabetic or at least there is a diabetic background. If one followed the patients with this disease but without diabetes long enough, say ten years, one might be able to demonstrate definite diabetes.

Cornu Cutaneum. Presented by DR. L. H. WINER, Minneapolis.

Mrs. H. D., aged 72, first noted a lesion on the right cheek two years ago, which has grown rapidly. She does not wish any therapy. The lesion is verrucous and hornified.

DISCUSSION

DR. STEPHAN EPSTEIN, Marshfield, Wis.: I certainly agree with the diagnosis of cornu cutaneum. Of course, properly speaking, this is not a diagnosis because cornu cutaneum may be a variety of lesions. It seems to me that in most cases of cornu cutaneum, the condition, usually less extensive than in this case, is plain keratosis, senile or otherwise; in some it develops on top of a chronic inflammation, like lupus vulgaris, or even on an old scar. However, there are primary squamous cell epitheliomas resembling cornu cutaneum. These sometimes are difficult to differentiate from senile keratosis even microscopically. On account of the possibility that this patient is suffering from a squamous cell epithelioma, I would urge her to have it removed surgically in spite of her age.

Glossitis Rhombica Mediana. Presented by Dr. J. F. Madden, St. Paul.

Mr. O. N., aged 43, stated that he first noted a bean-sized elevated red plaque in the midline of the posterior third of the tongue in 1938. The lesion grew steadily for one year and has not grown since. It is the size of a small olive and slightly elevated and has retained its reddish color. There are no accompanying subjective symptoms.

The Wassermann reaction of the blood was negative.

Fibrosarcoma. Presented by Dr. H. E. Michelson, Minneapolis.

A nodule was first noticed on the right side of the neck of this 10½ month old baby in November 1940. The lesion has been increasing rapidly in size. There is no history of a preexisting injury.

At the right angle of the jaw is a triangular reddish yellow hard nodular elevated plaque, 3.75 by 2 cm. in size. The surrounding skin is under tension. There are three similar circular lesions, each about 3 mm. in diameter, in the surrounding tissue.

(A histologic section was shown.)

News and Comment

DEATHS

Dr. Henry D. Niles, of New York, died on Aug. 27, 1941, as the result of an automobile accident.

CON

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